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# Respiratory Health Conditions and Ambient Ozone: A Case-Crossover Study

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## Abstract

**Context**: This research used International Classification of Diseases, 9th Revision (ICD-9) coding from 10 years of emergency department (ED) data (2, 951, 878 diagnosed visits) to identify diseases of the respiratory system (ICD-9: 460-519). The study estimates the potential associations of ED visits with ozone.

**Design**: The cases of the ED visits from this group (N=292, 285) were linked to the measurements of ambient ground-level ozone. A time-stratified case-crossover design was applied to match case and control periods. Conditional logistic regression was used to realize the case-crossover technique. Temperature and relative humidity were adjusted in the models in the form of natural splines.

**Results**: The results for diseases of the respiratory system (ICD-9: 460-519) confirmed a strong association between presentations and ambient ozone. Estimated odds ratios were positive and statistically significant for each considered lag (lag 0–7 days) of ozone exposure. Positive and statistically significant associations with ozone exposure were also obtained for the diseases of the skin and sense organs.

**Conclusion**: These results confirm associations between ambient ozone concentrations and respiratory disease presentations to EDs. Efforts to reduce ozone levels in the atmosphere may mitigate ED presentations to EDs for respiratory problems.

**Keywords:** Code; Emergency department; Humidity; Ozone; Respiratory; Temperature

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## Introduction

Environmental epidemiological studies examining the association among ambient air pollutants and health conditions have tended to focus on one, often broad, health outcome (e.g. cardiovascular disease) [1], or a panel of related health outcomes (e.g. diseases of the cardiovascular system, diseases of the respiratory system) [2]. Recent work, however, suggests that human health impacts extend beyond the respiratory and cardiovascular systems. Epidemiological studies have found associations between air pollutants and stroke, abdominal pain/appendicitis, depression, suicide, skin rash, cellulitis, and other conditions [3-14]. These results suggest that the health burden attributable to air pollution may be considerably greater than previously considered. Like several other authors we believe further examination of the short-term effects of air pollution on all conditions is warranted [14].

Given the emergence of associations among air pollutants and non-traditional health outcomes, an approach that examines the relationship among air pollutants and health effects that result in hospitalization (and hence can be tracked) without deciding a priori those diseases expected to be associated with the pollutants may be useful in identifying novel adverse health outcomes associated with pollutant exposure. Identified associations could then be further studied through focussed epidemiological and toxicological studies. The present study examined potential associations of ambient ground level ozone ($O_3$) with emergency department (ED) visits for respiratory conditions.

In addition, only for the comparison purpose, the study examined potential associations of ambient air pollution exposure to carbon monoxide (CO), nitrogen dioxide ($NO_2$), sulphur dioxide ($SO_2$), and particulate matter of median aerometric diameter less than 10 and 2.5 microns ($PM_{10}$, $PM_{2.5}$ respectively) with emergency department visits for health conditions categorized in 18 different groups. These groups were identified using the structure of the systematic health code system. The aim of this study was to assess the potential links between ambient ground-level ozone and respiratory diseases categorized using this high level classification.

The main hypothesis of this work is that "respiratory health problems" are strongly associated with exposure to ambient ground-level ozone. To investigate this thesis, this work contrasts the associations for 18 health condition groups with six ambient air pollutants.

# Method

## ED visits

ED visit data covering all five major acute care hospitals in the greater Edmonton region over a 10 year period (April 01, 1992–March 31, 2002) were obtained from Capital Health (now referred to as Alberta Health Services (AHS)–Edmonton Zone). Edmonton has an academic-focused health care system and is a part of one of the largest integrated health regions in Canada. The system provides complete health services to approximately one million residents. At the time, these hospitals each had an annual ED visit census ranging from approximately 45,000 to 60,000 patients. ED visits for specific health conditions were identified based on the discharge diagnosis using the International Classification for Diseases 9th revision (ICD-9) [15], coded by medical record nosologists. This study focuses on the ED visits for respiratory disease identified by using diagnosed cases with ICD-9: 460-519. In addition only for comparison purpose, all 18 groups of health problems were considered (see **Table 1**). The visits were date-tagged at the day of arrival to the ED. The analysis was restricted to diagnosed ED visits and identified by numerical ICD-9 code.

## Air Pollution and weather measurements

Air pollution data were obtained from the National Air Pollution Surveillance (NAPS) system using urban background fixed monitors with three stations (Northwest, Central and East) covering the city. The largest distance, realized between Northwest and East, is about 10 km. For a map of Edmonton displaying the station location and for further information regarding air pollution in Edmonton and the stations, please refer to the report "Air Quality Monitoring in Alberta 1994 Summary Report" [16].

When air pollution data were available from more than one monitoring site in the city, they were averaged. Days (for monitors) in which more than 6 measurements (representing one quarter of hourly values) were missing for the considered air pollutant among the 24 hourly measurements were excluded.

**Table 1** Health Conditions classified into 18 Groups according to ICD-9 Codes, Emergency Department visits, Edmonton, Canada, April 1992–March 2002.

| ICD-9 | Description | Cases |
|---|---|---|
| 001–139 | infectious and parasitic diseases | 416,876 |
| 140–239 | neoplasms | 11,044 |
| 240–279 | metabolic diseases/immunity disorders | 36,319 |
| 280–289 | diseases of the blood/blood-forming organs | 9,105 |
| 290–319 | mental disorders | 108,837 |
| 320–359 | diseases of the nervous system | 72,975 |
| 360–389 | diseases of the sense organs | 101,198 |
| 390–459 | diseases of the circulatory system | 134,490 |
| 460–519 | diseases of the respiratory system | 292,285 |
| 520–579 | diseases of the digestive system | 222,259 |
| 580–629 | diseases of the genitourinary system | 101,211 |
| 630–679 | complications of pregnancy/childbirth | 38,326 |
| 680–709 | diseases of the skin/subcutaneous tissue | 107,322 |
| 710–739 | diseases of the musculoskeletal system | 119,239 |
| 740–759 | congenital anomalies | 786 |
| 760–779 | conditions originating in the perinatal period | 2,521 |
| 780–799 | symptoms, signs, and ill-defined conditions | 350,001 |
| 800–999 | injury and poisoning | 827,084 |
| 001-999 | all | 2,951,878 |

Main exposure considered here is ground-level ozone. Other air pollutants are only used for comparative purpose [17].

Weather data were obtained from Environment Canada's weather archive. Environment Canada supplied hourly data for relative humidity and temperature (dry bulb) for the City of Edmonton. The daily levels of weather parameters, temperature and relative humidity were calculated by averaging hourly readings over 24 hour periods (24 measurements).

## Study design and statistical analysis

A case-crossover (CC) design that is useful for studying relationships that have short-time intervals for individual exposure, disease process, and induction periods was used. The CC design is an adaptation of the case–control design [18]. By definition, the cases acted as their own controls on a set of predefined control days proximate to the time they became cases. The CC approach mainly compares exposures at the event, here the time of ED visit (the case period) with a few periods when the ED visit did not occur (the control periods). A time-stratified approach to determine controls was widely adopted as it has been shown to produce unbiased conditional logistic regression estimates [19-21]. In the design, the controls are matched to case periods by day of week for the case period, with control periods selected in the same month and year. The same strategy was used here, thus 3 or 4 controls are present for each case. For example, if the case day was January 9, 2000, then January 2, 16, 23, and 30 would be considered control days. Thus, in this configuration, 4 control days would be available.

The generated results were calculated and presented as odds ratios (ORs) and their 95% confidence intervals (CI). The estimated ORs were reported for an increase in the concentration represented as an interquartile range (IQR=75th-25th values of percentiles) of air pollutant level. All components, air pollutant and meteorological factors, in the models were lagged by the same number of days, from 0 to 7. Temperature and relative humidity were used in the form of natural splines with 3 degrees of freedom. In the Appendix the code in SAS to realize this approach is presented.

## Results

**Table 1** displays the list of disease groupings identified by ICD-9 codes. It includes a short description of diseases in each group and the number of cases identified and used in the analysis. The analysis is focused on the respiratory health conditions for which 292,285 cases were identified.

Air pollution and meteorological specifications for the time period of the study are represented in **Table 2**. The table shows mean value, standard deviation, third quartile (Q3=75$^{th}$ percentile) and IQR (IQR=Q3–Q1). The results are reported for an increase of air pollutants by their corresponding (one) IQRs.

The main results are organized in the form of two figures. **Figure 1** illustrates the results for ED visits for respiratory condition in relation to ozone, two types of particulate matters and three gaseous air pollutants. The results for ozone are positive and statistically significant for all considered lagged exposures (lag 0-7 days), without evidence of a variation over time.

**Figure 2** provides a general look on the results. Black rectangles show effects where the estimated lower limit of the 95% CI for odds ratio was greater than 1. Thus it indicates positive and statistically significant association between the corresponding lagged (from 0 to 7) air pollutant and health conditions from the considered health group. As **Figure 1** showed for all lags the associations of respiratory diseases with ambient ozone are significant. The positive and statistically significant associations are also observed for disease of sense organs and skin (ICD-codes: 360-389 and 680-709, respectively). For exposure to ozone lagged by 3 and 5 days, positive association was obtained for diseases of the genitourinary system (ICD-9: 580–629), and for lag 0 (same day exposure) for injury and poisoning (ICD-9: 800–999).

Other results, including negative and statistically significant, are represented by a blank rectangle (white). Vertical lines (shown as break) identify those health groups where no positive

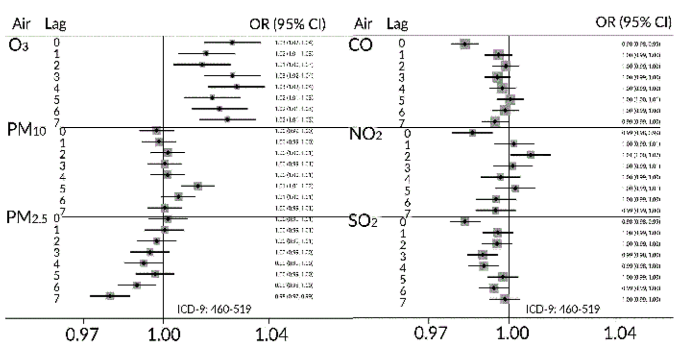


**Figure 1** ORs with their 95% CIs for ED visits for the respiratory conditions (ICD-9: 460-519).

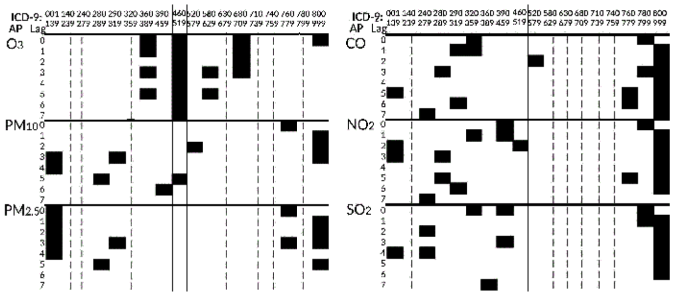


**Figure 2** The pattern of positive and statistically significant results (black rectangles).

associations were obtained. The associations were not observed for neoplasms, complication of pregnancy, diseases of the musculoskeletal system, and congenital anomalies. These health problems, as it's expected, don't have associations in short-term exposure. They are used as control health outcomes- the used method (CC) doesn't find any correlations between them and ambient air pollution exposures.

## Discussion

Studies examining adverse health effects of air pollution have historically focused on respiratory and cardiovascular disease. The focus on respiratory effects strongly affected the research field, to the extent that cardiac health conditions, which are now generally accepted as having a causal association with air pollution, were for a period considered as controls in studies examining the relationship between air pollution levels and respiratory conditions [22].

Using a large administrative database from one integrated geographic area in Western Canada and linked to reliable and valid Environment Canada data, the association between ozone levels and health conditions related to respiratory system was explored. As expected, increased hospital admissions for respiratory diseases were strongly associated with ozone [23]. Significant short-term effects were observed for ambient air pollution exposures on daily ED visits for cardiorespiratory diseases, as has been previously observed in numerous studies [1]. The range of health effects found to have associations to specific air pollutants is broad and defies simple mechanistic explanations. Considerable further work is required to confirm the findings in other datasets and to uncover the relevant biological mechanisms that underlie observed effects. The results for skin and sense organs are confirmed with the published literature [10, 24-27].

The limitations of this study are typical of this type of research. They include the adequacy of the model and impact of measurement error in the exposure and outcome variables. The fixed-site monitoring sites provide daily pollution exposures of ambient air pollution and are applied to represent average population exposure [28]. The fixed site monitors will not fully reflect variation in exposure among individuals. Numerous hypothesis tests were conducted, increasing the risk of false positive results; however, groupings of significant associations for some exposures (and lags) and health problems are observed, such as the association of admission for respiratory diseases

**Table 2** Number of days with Data, Mean, SD: Standard Deviation, Quartiles (Q3, IQR=Q3-Q1, 75th-25th percentile values, respectively) of Daily Average Concentrations of the Ambient Air Pollutants and Meteorological Factors. Edmonton, Canada, April 1992–March 2002.

| Variables (unit) | Days | Mean | SD | Q3 | IQR |
|---|---|---|---|---|---|
| O3 (ppb) | 3,652 | 18.6 | 9.3 | 25.2 | 14.0 |
| PM10 (µg/m3) | 2,813 | 22.6 | 13.1 | 28.3 | 15.0 |
| PM2.5 (µg/m$^3$) | 1,445 | 8.5 | 6.2 | 10.9 | 6.2 |
| CO (ppm) | 3,652 | 0.7 | 0.4 | 0.8 | 0.4 |
| $NO_2$ (ppb) | 3,652 | 21.9 | 9.4 | 27.6 | 12.8 |
| $SO_2$ (ppb) | 3,652 | 2.6 | 1.8 | 3.5 | 2.3 |
| Temperature (°C) | 3,652 | 3.9 | 11.9 | 13.9 | 17.9 |
| Humidity (%) | 3,652 | 66.0 | 13.6 | 75.6 | 18.5 |

and ozone, that are congruent with previous work. This analysis was conducted at a high level of disease classifications and as a result some of the grouped health conditions may not have a common response to air pollution exposure. It is quite possible that specific health conditions, when considered separately, may yield positive associations that in the present study are masked by grouping with other health conditions with neutral or negative associations. In practice, this should be verified for specific health outcomes. Further studies should focus on identifying subgroups within the ICD-9 (and/or ICD-10) classifications and examine their relation of air pollution exposures.

The main purpose of the presented work was to investigate the association between respiratory health conditions and ground-level ozone exposure. Evidence from observational studies strongly indicates that higher daily ozone levels are associated with increased asthma attacks, increased ED visits, increased hospital admissions, increased daily mortality, and other markers of morbidity related to respiratory health outcomes. As it was already mentioned above, for a specific sub group of these health conditions, the associations may be stronger than observed here for all cases diagnosed as ICD-9: 460-519. Such situation is observed for the associations between ozone and ED visits for lower respiratory condition, mainly bronchitis (ICD-9: 466, 490-492, 494, 496) [29]. The associations for ED visits for lower respiratory condition with ground-level ozone are stronger than the associations presented here. Without proper separation of the respiratory conditions with different pathophysiology, it is unknown whether the response is solely contributed by bronchitis. Based on the findings of the present report, it is also unknown whether respiratory diseases other than bronchitis have similar association. Also other respiratory conditions and never considered as having the associations with ozone can be triggered by higher ozone concentrations. This is another kind of limitation of this study.

In conclusion, the results presented here support the hypothesis that ED visits for a number of respiratory health problems are associated with ozone exposure. Breathing ground-level ozone can affect broad segments of the population. It can result in various respiratory health conditions.

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