

AIR POLLUTION AND DAILY EMERGENCY DEPARTMENT VISITS FOR DEPRESSION

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Abstract

Objectives: To investigate the potential correlation between ambient air pollution exposure and emergency department (ED) visits for depression. **Materials and Methods:** A hierarchical clusters design was used to study 27 047 ED visits for depression in six cities in Canada. The data used in the analysis contain the dates of visits, daily numbers of diagnosed visits, and daily mean concentrations of air pollutants as well as the meteorological factors. The generalized linear mixed models technique was applied to data analysis. Poisson models were fitted to the clustered counts of ED visits with a single air pollutant, temperature and relative humidity. **Results:** Statistically significant positive correlations were observed between the number of ED visits for depression and the air concentrations of carbon monoxide (CO), nitrogen dioxide (NO₂), sulphur dioxide (SO₂) and particulate matter (PM₁₀). The percentage increase in daily ED visits was 15.5% (95% CI: 8.0–23.5) for CO per 0.8 ppm and 20.0% (95% CI: 13.3–27.2) for NO₂ per 20.1 ppb, for same day exposure in the warm weather period (April–September). For PM₁₀, the largest increase, 7.2% (95% CI: 3.0–11.6) per 19.4 µg/m³, was observed for the cold weather period (October–March). **Conclusions:** The results support the hypothesis that ED visits for depressive disorder correlate with ambient air pollution, and that a large majority of this pollution results from combustion of fossil fuels (e.g. in motor vehicles).

Key words:

Air pollution, City, Cluster, Depression, Emergency department, Generalized linear mixed model, Relative humidity, Temperature

INTRODUCTION

Numerous studies have linked air pollution to human health. Notably, fine particulate matter has been linked to increased rates of hospitalization for cardiovascular and respiratory disease [1–3]. In addition, air pollution has been associated with increased rates of mortality [4,5].

Depression is a common illness with a multifactorial etiology comprising a combination of biological, psychological and social factors [6]. Emergency departments (ED) often encounter patients with depression who present with life threatening illness or injury, including suicidal

behaviour [7]. These are important health care encounters which consume considerable health care resources, so efforts to elucidate the causes of these presentations are warranted.

Recently, several studies have examined the common reasons for ED presentations and their correlation with air pollution. For example, ED visits for migraine headache and asthma have been linked to air pollutants in Canada [8,9]. Limited literature is available on the association between ambient air pollution exposure and ED visits for depression [10]. However, a recent study in Edmonton, Canada, has suggested that such a relationship may

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exist [11]. Notably, acute and frequent poisoning episodes have been linked with psychiatric sequelae [12]. A prospective longitudinal study of carbon monoxide poisoning concluded that CO poisoning results in significant depression and anxiety that can persist for at least 12 months [13]. As other studies have demonstrated, there are relationships between depression and exposure to air pollutants in the context of poisoning or occupational exposures [14–17]. However, the health consequences of exposures to relatively low ambient concentrations of air pollutants are not well understood.

The present work is a time-series study of emergency department (ED) visits for depression in six Canadian cities. Here, we have considered ambient air pollution and weather conditions as an exposure, and emergency department visits for depression as the health outcomes. Our hypothesis was that the number of ED visits for depression would increase with the increasing concentrations of ambient air pollutants.

MATERIALS AND METHODS

ED Visit

ED visit data were obtained from six cities in Canada: Edmonton, Halifax, Montreal, Ottawa, Toronto, and Vancouver. The data for Edmonton were composed of data sets from five different hospitals in the Capital Health region. In Toronto, the data from two different hospitals were studied separately, due to non-uniform coding methods. These data were labelled as Toronto and Sunnybrook. The other locations included only one hospital.

Depression Cases

ED visits for depression were identified based on a discharge diagnosis of depression using the International Classification for Diseases, 9th revision (ICD-9), rubric 296. In Edmonton, the ICD-9, rubric 311 was used to identify and record depression cases. In all cities, the discharge diagnosis was accompanied by a standardized string with the words “DEPRESSIVE DISORDER”. The visits were date-tagged at the day of arrival to the ED. In total, the analysis was based on 27 047 ED visits for depression

over a span of 13 709 days in 6 different cities i.e. days are summarized across the time periods and locations. The access to data was approved by the research ethics boards at each participating institution and the data, after de-identification, were transferred to the Health Canada team. No patient contact was made and patients could not be traced.

Air Pollution Measurements

Air pollution data were obtained from the National Air Pollution Surveillance (NAPS) system, and weather data from weather archive of the Environment Canada. We obtained data on carbon monoxide (CO), nitrogen dioxide (NO₂), ozone (O₃), sulfur dioxide (SO₂), and particulate matter with a mass median aerodynamic diameter of less than 10 and 2.5 microns (PM₁₀, PM_{2.5}, respectively). Daily mean values of pollutant concentrations, as an average of hourly readings (24 values), were used to represent the shared exposure of the population studied. The meteorological variables employed were temperature (dry bulb) and relative humidity. The daily mean as an average of hourly readings (24 measurements) was applied to represent these weather parameters. In the final models, the weather variables were treated as confounders.

Statistical Analysis

We applied the generalized linear mixed models (GLMM) technique on clusters [18–20]. We first defined the clusters for available data. The records of the data were clustered by the days of the week in the same month, in the same year, and in the same location. The data were grouped and analyzed according to the defined clusters. The clusters follow a hierarchical structure and dependency of days in a calendar-time relation and have embedded multilevel relations: days are nested in week days, week days are nested in months, and months are nested in years. According to this concept, visit days were grouped according to the specified nested relation {location, year, month, day of week}, which expresses the hierarchical structure. Such an approach allows us to unify the week day effects on the number of ED visits and to adjust for the day of the

week periodicity. The cluster structures absorb seasonal cycles and trends in a time-series of visits. The clusters also group the days with similar air pollution levels, where the pollutant concentrations are affected by human activities related to weekdays.

The independent variables in the constructed models were air pollutants, temperature and relative humidity measured on the same day, and the 1-day and 2-day lagged values. We considered four-level hierarchical formulations for random effects, whereby the clusters from the same month contain month-specific random effects and the clusters from the same year contain random year effects. We assumed a fixed slope and random intercept in the constructed models. The fixed slope option is the result of the assumption that the response to the exposure is the same for all clusters. The random intercept allows adjusting for different levels of counts on the clusters. This absorbs the cycles and trends in the time-series of the data.

To construct our models, we used the freely available R statistical software [21]. From this software, the *glmmPQL* function was used. An example of the model is shown below:

$$\begin{aligned} & \text{glmmPQL}(\text{fixed} = \text{Count} \sim \text{AirP}_n \\ & + \text{ns}(\text{Temp}_n, 3) + \text{ns}(\text{RHum}_1, 3), \\ & \text{random} = \text{list}(\text{location} = \sim 1, \text{year} \\ & = \sim 1, \text{month} = \sim 1, \text{day of week} = \sim 1)) \end{aligned}$$

In the model, the variable Count represents the daily number of ED visits for depression, AirP_n daily mean of air pollutant concentrations, Temp_n daily mean temperature, and RHum_n daily mean relative humidity, all lagged by n-days. Two meteorological variables were used in a non-linear form as natural splines (ns) with three degrees of freedom. Here, we used the same day exposure and 1- and 2-day lagged exposure. We conducted separate analyses for the whole period (January–December), warm period (April–September) and cold period (October–March) for the same day and 1-day and 2-day lagged values.

The results are reported as the percentage changes (% relative risk {RR}, i.e. excess risk) in ED visits for depression and their 95% confidence intervals (CI).

RESULTS

Table 1 contains the number of ED visits for depression by location. Due to the early starting date of the project, and the fact that five hospitals were included in the study, the highest number of ED visits for depression was observed in Edmonton. The observation periods were different in different locations, and as a consequence, the four-level hierarchical clusters (location, year, month, day of week) may have components for all the six cities or just for one city. Some data have missing values (no health data available); therefore, the starting date and the number of days with data was reported.

Table 1. The duration of the study periods (days) and the number of ED visits for depression by location

City	Starting date	Study period (days)	ED visits for depression n
Edmonton	April, 1992	3 652	15 556
Halifax	September, 1998	1 583	2 416
Montreal	January, 1997	2 191	4 472
Ottawa	April, 1992	3 075	1 795
Toronto	July, 2000	639	391
Sunnybrook	May, 1999	1 049	676
Vancouver	January, 1999	1 520	1 741
All cities	April, 1992	13 709	27 047

Table 2 gives the summary statistics of daily mean concentrations of air pollutants and the percentage of days for which ambient air pollution data were available. The mean values varied by city, with the highest levels of CO and NO₂ recorded at the Toronto locations. The highest concentrations of SO₂, O₃, and PM_{2.5} were recorded in Halifax, and of PM₁₀ in Montreal. These values represent the levels of ambient air pollutants in different locations. As a common level of exposure, the mean value for each pollutant among cities was chosen. The mean values were used to calculate the risks associated with air pollution in Canada.

Table 3 reports the percentage changes (%RR) in ED visits for depression and their 95% CI across the mean values of the ambient air pollutant levels for the whole time

Table 2. The mean concentrations of air pollutants and the percentage of all study days with data

City	CO (ppm)	%*	NO ₂ (ppb)	%	SO ₂ (ppb)	%	O ₃ (ppb)	%	PM ₁₀ (µg/m ³)	%	PM _{2.5} (µg/m ³)	%
Edmonton	0.7	100	21.9	100	2.6	99	18.6	100	22.6	77	8.5	39
Halifax	0.5	65	17.5	63	10.0	69	22.1	69	0	0	9.8	33
Montreal	0.5	100	18.4	100	4.8	100	18.3	100	25.8	50	8.6	88
Ottawa	0.9	100	18.8	100	3.9	99	17.5	99	20.1	12	6.5	31
Toronto	1.1	100	22.9	100	4.2	100	20.8	100	20.6	86	8.9	100
Sunnybrook	1.2	100	23.4	100	4.5	100	21.0	100	20.8	91	9.4	100
Vancouver	0.6	100	16.8	100	2.5	100	14.2	100	12.8	100	6.4	71
All cities	0.8	95	20.1	96	4.6	96	18.9	96	19.4	53	8.3	56

*The percentage (%) expresses fraction of days with data for the study period for city.

period (January–December), warm period (April–September) and cold period (October–March), respectively. The table indicates the risks associated with an increase in the level of air pollutant (exposure vs. no-exposure). Same day exposure to CO (% increase in RR = 6.9%), NO₂ (10.0%), SO₂ (2.6%), and PM₁₀ (6.4%) was found to correlate with ED visits for depression. There was a slight variation between the warm and cold weather periods; however, CO, NO₂, and PM₁₀ correlated with ED visits for depression in both the periods. For the whole time period, ozone, lagged by 2 days, correlated with a 3.9% increase in %RR (95% CI: 0.4–7.6).

Figure 1 shows the values of %RR for the six pollutants, lagged by 0, 1 and 2 days, and for the three time periods under study. The figure illustrates the relations for the same day exposure as the ED visits (lag 0) and 1 and 2 days before the visits. Among the pollutants associated with ED visits for depression, a waning of the effect can be observed over the lag period for each.

Figure 2 demonstrates the results for the same data, with the health outcomes as the ED visits for pulmonary problems (asthma, chronic obstructive pulmonary disease — COPD, respiratory inflammation) and cardiac problems (angina, cardiac dysrhythmia, congestive heart

Table 3. The percentage changes in adjusted relative risks (%RR) and their 95% confidence intervals (95% CI) for ED visits for depression, in relation to an increase in the mean concentrations of ambient air pollutants*

Pollutant	Period					
	whole		warm		cold	
	%RR	95% CI	%RR	95% CI	%RR	95% CI
CO	6.9	3.8, 10.1	15.5	8.0, 23.5	4.4	0.9, 8.1
NO ₂	10.0	6.6, 13.6	20.0	13.3, 27.2	6.4	2.1, 10.8
SO ₂	2.6	-0.1, 5.3	5.9	1.1, 11.0	1.5	-1.8, 5.0
O ₃	-4.0	-7.3, -0.6	-1.1	-5.9, 3.9	-8.3	-13.3, -3.1
PM ₁₀	6.4	3.6, 9.4	5.9	1.9, 10.0	7.2	3.0, 11.6
PM _{2.5}	2.3	-0.2, 4.7	2.6	-0.6, 5.9	1.9	-1.8, 5.9

* The results are presented for the whole period (January–December), warm period (April–September) and cold period (October–March).

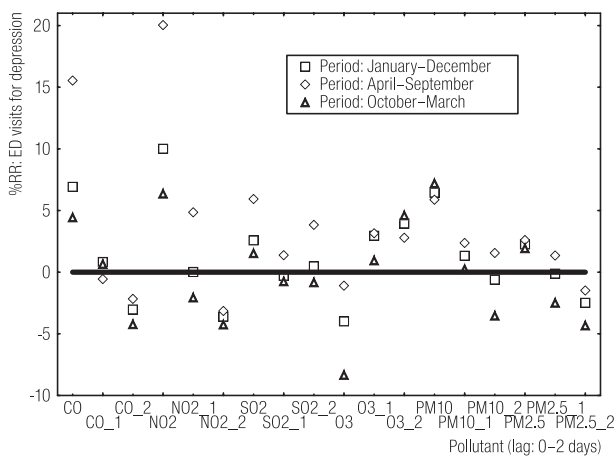


Fig. 1. The percentage changes in the relative risk (%RR) by pollutants (lagged by 0, 1 and 2 days) and time periods for ED visits for depression.

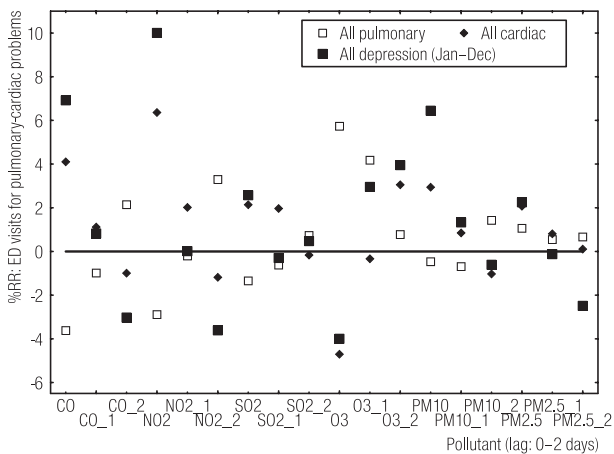


Fig. 2. The percentage changes in the relative risk (%RR) by pollutants (lagged by none, 1 and 2 days) and time periods for ED visits for pulmonary-cardiac problems.

failure — CHF). The pattern of the relationship between the air pollutants and ED visits for depression closely resembled that for ED visits for heart problems. However, the effect of air pollutants appears to be greater for the depression-related than for cardiovascular presentations to ED departments.

DISCUSSION AND CONCLUSIONS

In this study, significant short-term effects were observed for ambient air pollutant exposures on daily ED visits for depression in six cities in Canada. An air pollution event may result in acute health problems related to depression.

The highest percentage increase in ED visits was 20.0% for same day exposure to 20.1 ppb NO_2 recorded in the warm period (April–September). This analysis covers only the cases of depression, presumably more severe, where individuals seek ED treatment. In the light of the limited evidence in this area, verification of these correlations in other studies would be necessary.

There is toxicological evidence that gaseous and particulate air pollutants can adversely affect the brain and nervous system. Brain damage and severe neuropsychiatric symptoms can result from acute CO intoxication. At lower doses, CO exposure can lead to vision problems and decrements in hand-eye coordination and attention/vigilance, thus having impact on manual dexterity, the performance of complex tasks, and the ability to work or learn. The effects of CO on the central nervous system (CNS) are thought to be due to its interference with oxygen delivery to the brain. Interestingly, CO is also an endogenous neurotransmitter. It has become apparent that inhalation of particulate matter (PM) can have influence on the CNS. Recent work with experimental animals has provided evidence for neuropathological effects, including reduced dopaminergic neuron density in mice exposed to concentrated ambient particles (CAPs) [22], and changes in neurotransmitter levels in rats exposed by inhalation to CAPs [23]. There is some evidence from animal studies that inhaled particles, especially the ultrafine size fraction, may be able to distribute to the brain [24–26]. However, there is a lack of clinical research on PM-induced neurological effects in humans.

Ozone inhalation can also affect the CNS. Effects in experimental animals have been reported at moderate to high doses, approximately 120 ppb ozone and higher, and include behavioural alterations such as decreased motor activity and exploratory behaviour, memory deficits, and changes in neurotransmitter levels, electrical activity, sleep patterns and brain structure [27]. The sequelae of neurobehavioural, neurochemical and neurostructural events associated with ozone exposure is believed to be an indirect effect, probably initiated by the production of free radicals, oxidative by-products and inflammatory intermediates in both the peripheral and central nervous

systems. Evidence of ozone-induced neurological outcomes in humans is lacking; however, a recent study has shown a tentative link between ozone levels and suicidal behaviour [28]. Overall, there is a mounting toxicological evidence showing that exposure to gaseous and particulate air pollutants can cause adverse neurological effects ranging from behavioural changes to neuro-degeneration. This evidence, mainly from experimental animal studies, provides a level of biological plausibility to the notion that exposure of human populations to air pollutants may result in neurochemical or neuropathological changes that could potentially manifest as or contribute to depression, suicide ideation or related psychological outcomes [29–31].

The findings of this study need to be interpreted in light of the inherent limitations of the data. The hospitals are located in large cities in Canada. ED visits for depression might be affected by many factors related to large cities and the results may not be generalized to smaller cities or rural areas [32]. Misclassification of the cause of ED visits, underreporting in the hospital registry system, and the low frequency of visits might have influenced the ability to detect correlations. The limitations of this study are also typical of this type of research. They include the adequacy of the model and the impact of measurement error in the exposure and health outcome variables. The proposed approach is a new technique to assess the impact of ambient conditions on the health outcomes. The models applied in this study were based on the structure {location, year, month, day of week}. In addition, an analysis was performed for each location separately (to check sensitivity) and the results were pooled [33].

The results from the meta-analysis (data are not shown here) were very similar to those reported in Table 3. More detailed analysis was performed on the five-site Edmonton data [11] providing some reassurance of congruence. In addition, for Edmonton data, we performed the case-crossover analysis [34] for females in the warm period and sulphur dioxide. We defined the sequence of 77 of the overlapping age intervals ([0, 9], [1, 10], [2, 11], ..., [76, 85], of 10 years' each). Figure 3 shows the obtained odds ratios and 95% CIs for an increase in the interquartile range (2.3 ppb). The figure illustrates that

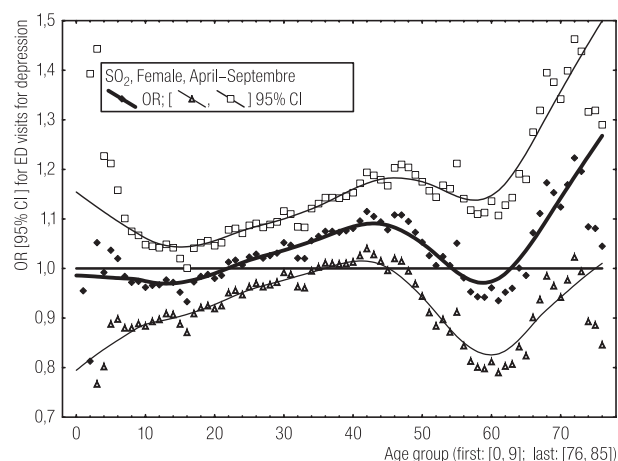


Fig. 3. The odds ratios (OR) and 95% CIs for the sequence of 77 overlapping age intervals (of 10 years' each).

the correlation increases with the patients' age [34]. Finally, it should be noted that using these methods we are only able to demonstrate the correlation between exposure and the number of ED visits. We cannot demonstrate causality, but have shown a correlation which may suggest a trigger for emergency admissions for depression [35]. We demonstrated that an increase in ambient air pollution level was associated with an increased number of ED visits.

The results support the hypothesis that ED visits for depressive disorder correlate with ambient air pollution, and that a large majority of this air pollution results from combustion of fossil fuels (e.g., in motor vehicles). This effect differs in the warm and cold weather periods in Canada.

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