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Urban Air Pollution and Emergency Department Visits for Cardiac and Respiratory Diseases

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Abstract

Air pollution affects various aspects of human health. Here, the associations between the number of emergency department visits for circulatory and respiratory problems and ambient air pollution in Toronto, Canada, in the period between April 2004 and December 2015 were studied. The health data were linked with urban air pollution data and weather factors. The conditional Poisson regression models were built for 18 strata (sex, age group, season), 8 exposure factors (air pollutants, indexes), and their 15 lags (0-14 days). Circulatory problems: the associations were intensified in the cold period (October - March) and were associated with the air quality health index (AQHI). The estimated relative risks for all patients in the cold period, for an increase of the AQHI by 1, at lags 0, 1, and 2 were 1.017 and 95% confidence interval (1.010, 1.024), 1.014 (1.007, 1.021), and 1.009 (1.002, 1.016). Respiratory problems: the analogous results for ozone and its increase by 12.8 ppb at lags 3, 4, and 5 were 1.052 (1.033, 1.161), 1.039 (1.020, 1.121), and 1.027 (1.008, 1.082). It was observed that exposure to certain air pollutants (nitrogen dioxide, ozone, and the AQHI index) are associated with increased emergency department visits in both cardiac and respiratory health problems.

Keywords
Ambient air pollution; emergency; cardiac; health; respiratory

1. Introduction

The crowding of emergency departments (ED) has been shown to influence higher mortality rates, poorer patient outcomes or re-hospitalization and other detriments [1-3]. The Canadian Institute for Health Information (CIHI) reports that the top three most common emergency department visits are for pulmonary and circulatory problems, specifically pneumonia, chronic obstructive pulmonary disease (COPD), and heart failure [4]. According to the Center for Disease Control and Prevention's National Hospital Ambulatory Medical Care Survey from 2017 (https://www.cdc.gov/nchs/data/nhamcs/web_tables/2017_ed_web_tables-508.pdf) diseases of respiratory and circulatory nature constituted 27.5% of ED visits in the United States. An improved understanding of ED visits may allow hospitals to improve diagnostic and treatment efficiency. A significant association between worse ambient air quality and ED visits, morbidity and mortality has been established [5].

The presented work proposes a more insightful method to analyse ED visits for cardiorespiratory health problems. The data analysed originate from a large urban area with intensive vehicle traffic. In this analysis we do not categorize health conditions, but rather analyse all cardiac and all respiratory health problems.

Here we test the hypothesis that ambient air pollution concentration level changes are associated with the number of ED visits related to cardiovascular and respiratory health conditions based on particular combinations of age group, sex, and seasons. The basis of the hypothesis is rooted in demonstrated impacts of certain air pollutants on circulatory and respiratory problems. Numerous studies have shown relationships between air pollutants and acute or chronic circulatory diseases via lung inflammation [6-8], blood borne mediators, neuroendocrine activation, or particle translocation [9]. The same can be said for respiratory diseases, where air pollution can be linked to higher risk for patients with asthma, COPD, lung cancer, or for those at increased risk of respiratory infection [10]. The PubMed search with the terms "air pollution cardiac" gives 3,824 publications and with "air pollution respiratory" gives 13,230 publications. The Integrated Science Assessments (EPA, https://www.epa.gov/isa) presents a potential biological pathway for each air pollutant considered in this work. This paper focuses on the short-term acute effects of air pollution, and selecting a time unit of one day.

2. Materials and Methods

We choose to group all diseases in the respective circulatory and respiratory categories (International Classification of Diseases, Tenth Revision - ICD-10 - codes I00-I99 and J00-J99, respectively) as a collective, rather than investigate specific conditions. The goal of this paper is to investigate the correlations of the ED visit counts that are classified in these two categories with the variations in air pollution, using a large urban agglomeration in the city of Toronto, Canada, as the location of the study.

2.1 Health Data

The National Ambulatory Care Reporting System (NACRS 2020) database was used to obtain data concerning the diagnosed emergency department visits in Toronto, Canada for the 4,292 days in the period between April 1st 2004 and December 31st 2015. The health cases where the primary cause of visit was categorized in the International Classification of Diseases: ICD-10 codes I00-I99 and J00-J99 (Chapter IX: "Diseases of the circulatory system", Chapter X: "Diseases of the respiratory system"), respectively, were extracted from the database. The health data were organized as daily counts of ED visits.

2.2 Environmental Data

Data on six ambient air pollutants were retrieved from the National Air Pollution Surveillance (NAPS) Program (managed by Environmental and Climate Change Canada) Canada-Wide Air Quality Database (CWAQD) for the same period. The pollutants considered separately are carbon monoxide (CO), nitrogen dioxide (NO_2), ground-level ozone (O_3, as a daily average, O_3-h8, as a maximum eight-hour average of ozone), fine particulate matter ($PM_{2.5}$), and sulfur dioxide (SO_2). These datasets have been used in previous epidemiological multi-sites study [11].

To account for multipollutant exposures, two air quality indexes (AQHI and AQHIX) were calculated (see Table 1). The Air Quality Health Index (AQHI) is determined by the following formula, developed by Stieb et al. [12].

$$AQHI = \frac{1000}{10.4} \times (e^{0.000537*O3} + e^{0.000871*NO2} + e^{0.000487*PM2.5} - 3).$$

Table 1 summarizes statistics on air pollutants, temperature, and relative humidity in Toronto.

Table 1 Statistics on environmental factors (in 4,292 days). Toronto, Canada, 2004 - 2015.

Factors	Units	Min	Q1	Median	Mean	Q3	Max
PM25	g/m^3	0.1	4.7	7.1	8.9	11.2	65.5
NO_2	ppb	3.2	11.1	15.0	16.1	19.9	59.8
O_3	ppb	1.7	16.8	23.0	23.5	29.6	62.1
O_3H8	ppb	9.0	33.0	41.0	43.7	52.0	107.0
SO_2	ppb	0.0	0.5	1.0	1.4	1.7	12.0
CO	ppm	0.0	0.2	0.2	0.3	0.3	1.1
AQHI	number	1.0	2.4	2.9	3.0	3.4	7.6
AQHIX	number	1.6	3.6	4.2	4.4	5.1	10.3
Temperature	°C	-22.2	1.7	10.0	9.5	18.4	31.2
Relative Humidity	%	31.7	63.9	70.9	70.7	78.2	98.8

Notes. Min - minimum, Max -maximum, Q1-25th percentile, Q3-75th percentile.

The AQHI allows the estimate of risk associated with the ambient air quality to the general public and persons at risk using the three most prevalent pollutants (O_3, NO_2, and $PM_{2.5}$). While it is typically rounded to the nearest integer (1-10,10+) in this study no rounding was performed for analysis. The AQHIX is used to account for the combination of O_3H8 (an eight-hour average of O_3),

NO_2 and $PM_{2.5}$, calculated using the same formula. This index permits us to suppress the impact of O_3 concentrations on AQHI associations.

2.3 Statistical Approach

Given the nature of the available data, a time stratified case-crossover technique was deemed most appropriate, as it controls for the time-invariant factors characteristic of each individual case. These confounders can be comorbidities, smoking, socioeconomic position, employment situation, and others. To eliminate the bias resulting from time-trends, the time-stratified design was realized and thus all similar weekdays within one month were grouped together. This methodology also allows the separation of strata such as “male” or “female” by seasonality, here identified as “cold” (October-March) and “warm” (April-September), to highlight the elevated risk to health when air pollutant effects are exacerbated by temperature and humidity. Temperature and relative humidity was incorporated into the model in the form of natural splines with three degrees of freedom. The generalized non-linear model procedure (the gnm package) with the “quasipoisson” option in R statistical software (v. 4.0; 2020, The R Foundation for Statistical Computing) is used and estimates the coefficients and their standard errors for the considered air pollutants [13-16]. In this work, 2,160 statistical models are constructed for respiratory and cardiac health conditions. We applied the following statistical models

```
modelED <- gnm(EDCounts ~ AirPL + ns(TempL,3) + ns(RHumL,3), data=dataEDvisits, family=quasipoisson, eliminate=factor(Cluster)).
```

The quasi-Poisson regression is applied to model an overdispersed count variable. Here air pollutant (AirPL), weather factors (temperature and relative humidity, TempL, RHumL), are lagged by the same number of days (L). Here the lagged exposure by L days means that the values of air pollutants and weather factors are used from previous L days. The hierarchical Cluster has the form <year:month:day of week>. Such cluster contains 4 or 5 days. There are 1008 of such hierarchical levels (2004:1:1, …, 2015:12:7). This structure of the clusters allows to control for time and its impact. Relative risk is calculated using the estimated coefficient for AirPL. The gnm package realizes Generalized Non-Linear Models technique.

The relative risk (RR) was calculated for each stratum at every lag and every pollutant measure, but to quantify the strength of the most significant associations, only the strongest relative risks are shown. The RR values with their 95% confidence intervals are expressed per interquartile range. All these values are listed in supplementary materials. A p-value less than 0.05 was considered statistically significant. The Health Canada Research Ethic Board determined that the study is IRB exempt, given that patient data were pre-existing and de-identified.

3. Results

In the period of the study, a total of 484,967 cases categorized in ICD codes I00-I99 (diseases of the circulatory system) and 852,624 cases in ICD codes J00-J99 (diseases of the respiratory system) were recorded. 18 strata were used to separate cases by sex, age group and season. This allows identification of subgroups most affected by air pollution exposures.

Table 2 and Table 3 summarize the case count for each stratum in the circulatory disease categories and respiratory, respectively. Classified by sex were 235,301 male and 249,666 female circulatory disease cases over the same period. Classified by sex were 421,903 female and 430,721 male respiratory cases in the studied period. It should be noted that in the case of kids (patients younger than 11 year of age, Table 2) for circulatory diseases the number of visits is very small. In this regard there may be a statistical power problem. Table 3 summarizes statistics on air pollutants, temperature, and relative humidity in Toronto.

Table 2 Statistics on emergency department (ED) visits for all cardiac problems (ICD-10 codes: I00-I99). Toronto, Canada, April 2004 - December 2015.

Person/Age/Season	ED visits	Min	Q1	Median	Mean	Q3	Max
All	484,967	49	89	119	113.0	133	177
Female	235,301	19	45	56	54.8	64	96
Male	249,666	21	45	61	58.2	70	97
Warm All	246,331	50	88	118	112.2	132	174
Warm Female	119,641	19	45	56	54.5	64	96
Warm Male	126,690	21	45	61	57.7	69	93
Cold All	238,636	49	90	120	113.9	135	177
Cold Female	115,660	20	46	56	55.2	65	95
Cold Male	122,976	22	45	61	58.7	71	97
Age 0-10 All	1,764	0	0	1	0.9	1	6
Age 0-10 Female	1,286	0	0	0	0.3	0	4
Age 0-10 Male	1,990	0	0	0	0.5	1	5
Age 11-60 All	169,020	10	30	40	39.4	48	79
Age 11-60 Female	73,271	1	13	17	17.1	21	43
Age 11-60 Male	95,749	3	17	23	22.3	28	51
Age 60+All	312,671	27	59	75	72.9	86	120
Age 60+ Female	160,744	10	31	38	37.5	44	66
Age 60+ Male	151,927	10	28	36	35.4	43	65

Notes. Min - minimum, Max -maximum, Q1-25th percentile, Q3-75th percentile.

Table 3 Statistics on ED visits for all respiratory problems (ICD-10 codes: J00-J99). Toronto, Canada, April 2004 - December 2015.

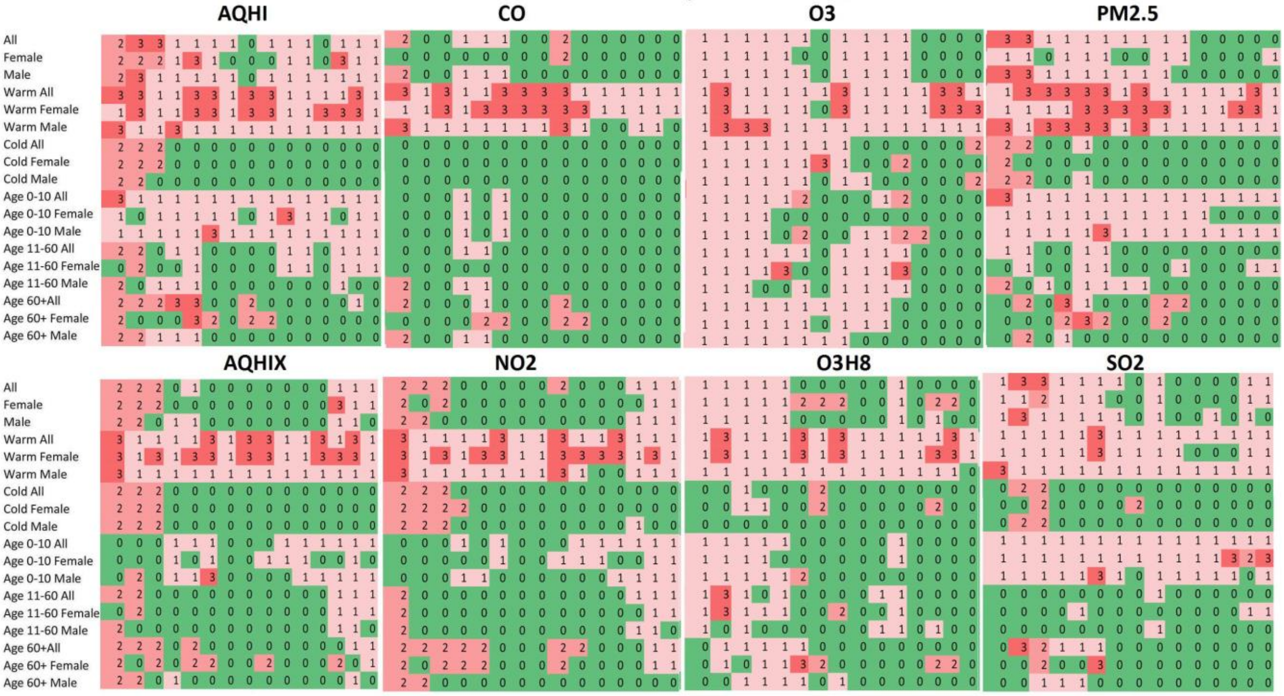
Person/Age/Season	ED visits	Min	Q1	Median	Mean	Q3	Max
All	852,624	86	161	188	198.7	220	751
Female	421,903	35	78	92	98.3	109	398
Male	430,721	39	82	96	100.4	113	358
Warm All	376,931	86	145	167	171.6	193	346
Warm Female	184,694	35	70	82	84.1	95	180
Warm Male	192,237	39	74	85	87.5	99	178
Cold All	475,693	125	185	209	227	244	751
Cold Female	237,209	53	90	103	113.2	123	398
Cold Male	238,484	51	94	106	113.8	124	358
Age 0-10 All	222,107	12	37	48	51.8	62	275
Age 0-10 Female	91,080	2	14	19	21.2	26	124

Age 0-10 Male	131,027	4	22	29	30.5	37	162
Age 11-60 All	434,200	42	83	95	101.2	112	426
Age 11-60 Female	227,051	17	42	49	52.9	59	237
Age 11-60 Male	207,149	13	39	46	48.3	54	189
Age 60+All	196,317	14	37	43	45.7	51	188
Age 60+ Female	103,772	6	18	23	24.2	28	114
Age 60+ Male	92,545	5	17	21	21.6	25	76

Notes. Min - minimum, Max -maximum, Q1-25th percentile, Q3-75th percentile.

To show the associations between the ED visits by strata and air pollutants (lags), their positive and statistically significant correlations are presented in Figures 1, 2, 3, and 4. Other associations (negative and none) are shown as a zero. The significance is defined as a p-value < 0.05. Using a p-value <0.001 rather than a p-value<0.05 as a criterion, 61 cases persist among 294 positive, and 420 among 919 positive, i.e., 20.7% and 45.5%, for circulatory and respiratory ED visits, respectively.

Figure 1 shows all statistically significant positive correlations between pollution and ED visits considered by a stratum and a lag for a particular pollutant for both circulatory and respiratory cases. Positive correlations for respiratory cases are indicated with a 1, and circulatory cases with a 2. A strata/lag combination showing 3 indicates an overlap of positive correlations for both respiratory and circulatory cases. If both are not positive, the cell contains a 0. All associations, including negative, can be found in Supplementary Materials (Figure e1 (Cardiac) and Figure e2 (Respiratory)), as well as the corresponding values of numerical estimations of slope and associated standard error (files CARDIACToronto.csv, RESPIRATORYToronto.csv) at https://github.com/szyszkowiczm/CardioRespirTORONTO. The columns in these figures represent sequential lags (from 0 to 14 days). In all presented figures colors are used to ease visualization of association counts, where a darker red indicates a larger association count in terms of the criteria not featured on one of the table axes (either strata, lags, or pollutants). The corresponding figures are presented in the referenced Supplementary Materials. These materials also include histograms of the considered ambient air pollutants, temperature, and relative humidity. The map of the city of Toronto which shows population density and the locations of monitor stations is also provided. Two figures, Figure e3 (RR, Cardiac, NO_2) and Figure e4 (RR, Respiratory, O_3), which present a forest plot for lags from 0 to 3 for nitrogen dioxide and ozone are given.



AQHI

All	2	3	3	1	1	1	1	0	1	1	1	0	1	1	1
Female	2	2	2	1	3	1	0	0	0	1	1	0	3	1	1
Male	2	3	1	1	1	1	1	0	1	1	1	1	1	1	1
Warm All	3	3	1	1	3	3	1	3	3	1	1	1	1	3	1
Warm Female	1	3	1	1	3	3	1	3	3	1	1	3	3	3	1
Warm Male	3	1	1	3	1	1	1	1	1	1	1	1	1	1	1
Cold All	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Cold Female	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Cold Male	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0
Age 0-10 All	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Age 0-10 Female	1	0	1	1	1	1	1	0	1	3	1	1	0	1	1
Age 0-10 Male	1	1	1	1	1	3	1	1	1	1	1	1	1	1	1
Age 11-60 All	2	2	0	1	1	0	0	0	0	1	1	0	1	1	1
Age 11-60 Female	0	2	0	0	1	0	0	0	0	1	1	0	1	1	1
Age 11-60 Male	2	0	1	1	1	0	0	0	0	0	0	0	1	0	0
Age 60+All	2	2	2	3	3	0	0	2	0	0	0	0	0	1	0
Age 60+ Female	2	0	0	0	3	2	0	2	2	0	0	0	0	0	0
Age 60+ Male	2	2	1	1	1	0	0	0	0	0	0	0	0	0	0

CO

All	2	0	0	1	1	1	0	0	2	0	0	0	0	0	0
Female	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0
Male	2	0	0	1	1	1	0	0	0	0	0	0	0	0	0
Warm All	3	1	3	1	1	3	3	3	3	1	1	1	1	1	1
Warm Female	1	1	3	1	3	3	3	3	3	3	1	1	1	1	1
Warm Male	3	1	1	1	1	1	1	1	3	1	0	0	1	1	0
Cold All	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cold Female	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cold Male	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Age 0-10 All	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0
Age 0-10 Female	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0
Age 0-10 Male	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0
Age 11-60 All	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
Age 11-60 Female	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Age 11-60 Male	2	0	0	1	1	0	0	0	0	0	0	0	0	0	0
Age 60+All	2	0	0	0	1	0	0	0	2	0	0	0	0	0	0
Age 60+ Female	0	0	0	0	2	2	0	0	2	2	0	0	0	0	0
Age 60+ Male	2	0	0	1	1	0	0	0	0	0	0	0	0	0	0

O3

All	1	1	1	1	1	1	0	1	1	1	1	0	0	0	0
Female	1	1	1	1	1	0	0	1	1	1	1	0	0	0	0
Male	1	1	1	1	1	1	0	1	1	1	1	0	0	0	0
Warm All	1	3	1	1	1	1	1	3	1	1	1	1	3	3	1
Warm Female	1	3	1	1	1	1	0	3	1	1	1	1	3	3	3
Warm Male	1	3	3	3	1	1	1	1	1	1	1	1	1	1	1
Cold All	1	1	1	1	1	1	1	1	0	0	0	0	0	0	2
Cold Female	1	1	1	1	1	1	3	1	0	0	2	0	0	0	0
Cold Male	1	1	1	1	1	1	0	1	1	0	0	0	0	0	2
Age 0-10 All	1	1	1	1	1	2	0	0	0	1	2	0	0	0	0
Age 0-10 Female	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0
Age 0-10 Male	1	1	1	1	0	2	0	0	1	1	2	2	0	0	0
Age 11-60 All	1	1	1	1	1	1	0	1	1	1	1	0	0	0	0
Age 11-60 Female	1	1	1	1	3	0	0	1	1	1	3	0	0	0	0
Age 11-60 Male	1	1	1	0	0	1	0	1	1	1	1	0	0	0	0
Age 60+All	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0
Age 60+ Female	1	1	1	1	1	1	0	1	1	1	0	0	0	0	0
Age 60+ Male	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0

PM2.5

All	3	3	1	1	1	1	1	1	1	1	0	0	0	0	0
Female	1	1	0	1	1	1	0	0	1	1	0	0	0	0	1
Male	3	3	1	1	1	1	1	1	1	0	0	0	0	0	0
Warm All	1	3	3	3	3	3	1	3	1	1	1	1	1	3	1
Warm Female	1	1	1	1	3	3	3	3	3	1	1	1	3	3	1
Warm Male	3	1	3	3	3	3	1	3	1	1	1	1	1	1	1
Cold All	2	2	0	0	1	0	0	0	0	0	0	0	0	0	0
Cold Female	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cold Male	2	2	0	0	1	0	0	0	0	0	0	0	0	0	0
Age 0-10 All	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Age 0-10 Female	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0
Age 0-10 Male	1	1	1	1	1	3	1	1	1	1	1	1	1	1	1
Age 11-60 All	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0
Age 11-60 Female	0	1	0	0	1	1	0	0	0	1	0	0	0	1	1
Age 11-60 Male	2	0	1	0	1	1	1	1	0	0	0	0	0	0	0
Age 60+All	0	2	0	3	1	0	0	0	2	2	0	0	0	0	0
Age 60+ Female	0	0	0	2	3	2	0	0	2	0	0	0	0	0	0
Age 60+ Male	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0

AQHIX

All	2	2	2	0	1	0	0	0	0	0	0	0	1	1	1
Female	2	2	2	0	0	0	0	0	0	0	0	0	3	1	1
Male	2	2	0	1	1	0	0	0	0	0	0	0	1	1	0
Warm All	3	1	1	1	1	3	1	3	3	1	1	3	1	3	1
Warm Female	3	1	3	1	3	3	1	3	3	1	1	3	3	3	1
Warm Male	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Cold All	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Cold Female	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Cold Male	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Age 0-10 All	0	0	0	1	1	1	0	0	0	1	1	1	1	1	1
Age 0-10 Female	0	0	0	1	0	1	0	0	1	1	1	0	0	1	0
Age 0-10 Male	0	2	0	1	1	3	0	0	0	0	1	1	1	1	1
Age 11-60 All	2	2	0	0	0	0	0	0	0	0	0	0	1	1	1
Age 11-60 Female	0	2	0	0	0	0	0	0	0	0	0	0	1	1	1
Age 11-60 Male	2	0	0	0	0	0	0	0	0	0	0	0	1	1	0
Age 60+All	2	2	2	0	2	0	0	0	0	0	0	0	0	1	1
Age 60+ Female	2	0	2	0	2	2	0	0	2	0	0	0	2	0	1
Age 60+ Male	2	2	0	1	0	0	0	0	0	0	0	0	0	1	0

NO2

All	2	2	2	0	0	0	0	0	2	0	0	0	1	1	1
Female	2	0	2	0	0	0	0	0	0	0	0	0	0	1	1
Male	2	2	0	0	0	0	0	0	0	0	0	0	1	1	1
Warm All	3	1	1	1	1	3	1	1	3	1	1	3	1	1	1
Warm Female	3	1	3	1	3	3	1	1	3	3	3	3	1	3	1
Warm Male	3	1	1	1	1	1	1	1	3	1	0	0	1	1	1
Cold All	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Cold Female	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0
Cold Male	2	2	2	0	0	0	0	0	0	0	0	0	1	0	0
Age 0-10 All	0	0	0	1	0	1	0	0	0	1	1	1	1	1	1
Age 0-10 Female	0	0	0	0	0	1	0	0	1	1	1	0	0	1	1
Age 0-10 Male	0	0	0	1	1	0	0	0	0	0	0	1	1	1	1
Age 11-60 All	2	0	0	0	0	0	0	0	0	0	0	0	1	1	1
Age 11-60 Female	2	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Age 11-60 Male	2	0	0	0	0	0	0	0	0	0	0	0	1	1	0
Age 60+All	2	2	2	2	2	0	0	0	2	2	0	0	0	1	1
Age 60+ Female	2	0	2	2	2	0	0	0	2	0	0	0	0	1	1
Age 60+ Male	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0

O3H8

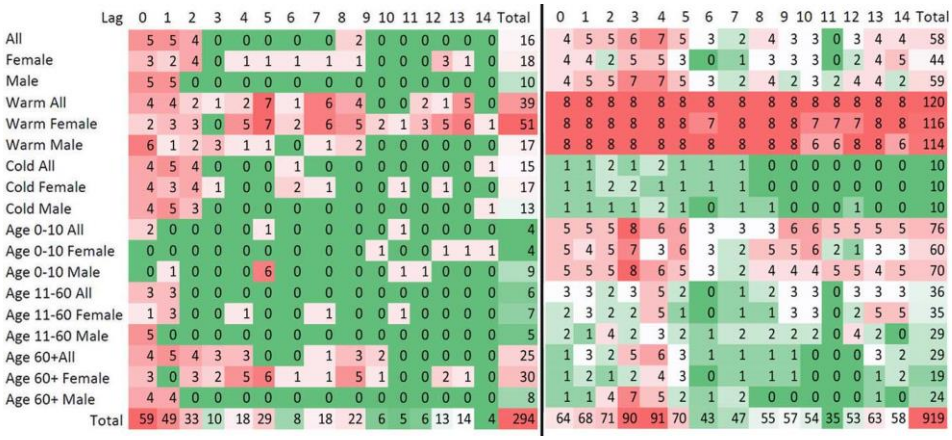
All	1	1	1	1	1	0	0	0	0	0	1	0	0	0	0
Female	1	1	1	1	1	2	2	2	0	0	1	0	2	2	0
Male	1	1	1	1	1	0	0	0	0	0	1	0	1	0	0
Warm All	1	3	1	1	1	3	1	3	1	1	1	1	1	3	1
Warm Female	1	3	1	1	1	3	1	3	1	1	1	1	3	3	1
Warm Male	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
Cold All	0	0	1	0	0	0	2	0	0	0	0	0	0	0	0
Cold Female	0	0	1	1	0	0	2	0	0	0	0	0	2	0	0
Cold Male	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Age 0-10 All	1	1	1	1	1	0	0	0	0	0	1	0	0	0	0
Age 0-10 Female	1	1	1	1	0	0	0	0	0	0	1	0	0	0	0
Age 0-10 Male	1	1	1	1	1	2	0	0	0	0	0	0	0	0	0
Age 11-60 All	1	3	1	0	1	0	0	0	0	1	1	0	0	0	0
Age 11-60 Female	1	3	1	1	1	0	0	2	0	0	1	0	0	0	0
Age 11-60 Male	1	0	1	0	0	0	0	0	0	1	1	0	1	0	0
Age 60+All	0	1	1	1	1	1	0	0	0	0	0	0	0	0	0
Age 60+ Female	0	1	0	1	1	3	2	0	0	0	0	0	2	2	0
Age 60+ Male	0	0	1	1	1	1	0	1	0	0	0	0	0	0	0

SO2

All	1	3	3	1	1	1	1	0	1	0	0	0	0	1	1
Female	1	1	2	1	1	1	0	0	1	0	0	0	0	1	1
Male	1	3	1	1	1	1	1	0	1	0	0	1	0	1	0
Warm All	1	1	1	1	1	3	1	1	1	1	1	1	1	1	1
Warm Female	1	1	1	1	1	3	1	1	1	1	0	0	0	1	1
Warm Male	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Cold All	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Cold Female	0	0	2	0	0	0	0	2	0	0	0	0	0	0	0
Cold Male	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Age 0-10 All	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Age 0-10 Female	1	1	1	1	1	1	1	1	1	1	1	1	3	2	3
Age 0-10 Male	1	1	1	1	1	3	1	0	1	1	1	1	1	0	1
Age 11-60 All	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Age 11-60 Female	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1
Age 11-60 Male	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Age 60+All	0	3	2	1	1	1	0	0	0	0	0	0	0	0	0
Age 60+ Female	0	0	2	0	0	3	0	0	0	0	0	0	0	0	0
Age 60+ Male	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0

Figure 1 The associations between pollution and ED visits by a stratum, pollutant and lags (from 0 to 14 days) for ICD Codes I00-I99 (Circulatory) indicated with a 2 and for ICD Codes J00-J99 (Respiratory) indicated with a 1. If both statistical significance associations overlap, a 3 is indicated. Other associations are shown by a 0.

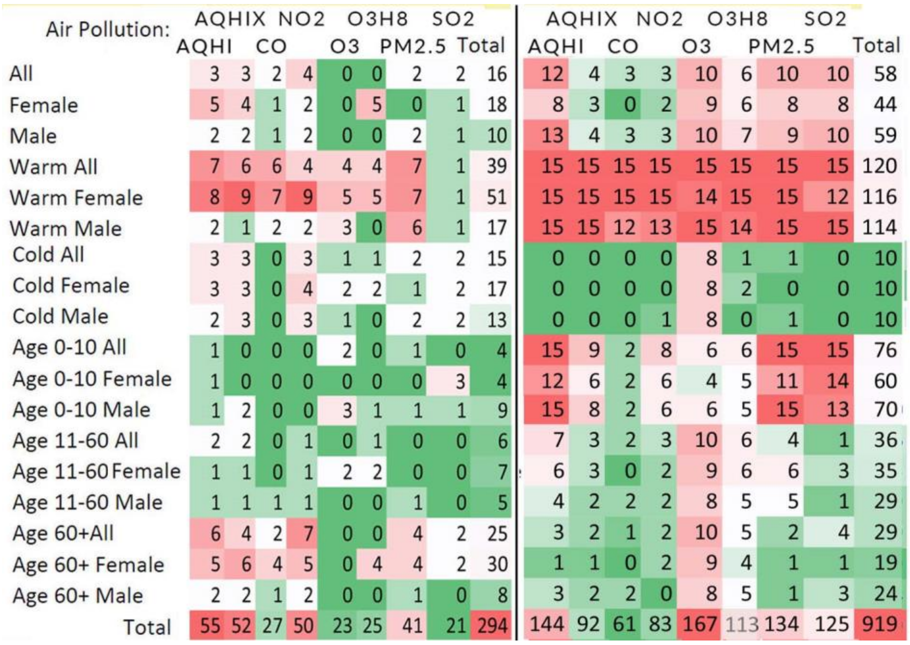
Figure 2 illustrates a summary of both the circulatory (left) and respiratory (right) counts of models with statistically significant associations between pollution and ED visit considered for a particular stratum and every lag used (0 to 14). In other words, it shows the number of positive statistically significant associations between cardiovascular and respiratory ED visits and all air pollutants and AQHI combined.



Lag	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
All	5	5	4	0	0	0	0	0	2	0	0	0	0	0	0	16	4	5	5	6	7	5	3	2	4	3	3	0	3	4	4	58
Female	3	2	4	0	1	1	1	1	1	0	0	0	3	1	0	18	4	4	2	5	5	3	0	1	3	3	3	0	2	4	5	44
Male	5	5	0	0	0	0	0	0	0	0	0	0	0	0	0	10	4	5	5	7	7	5	3	2	4	2	3	2	4	4	2	59
Warm All	4	4	2	1	2	7	1	6	4	0	0	2	1	5	0	39	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	120
Warm Female	2	3	3	0	5	7	2	6	5	2	1	3	5	6	1	51	8	8	8	8	8	8	7	8	8	8	7	7	7	8	8	116
Warm Male	6	1	2	3	1	1	0	1	2	0	0	0	0	0	0	17	8	8	8	8	8	8	8	8	8	8	6	6	8	8	6	114
Cold All	4	5	4	0	0	0	1	0	0	0	0	0	0	0	1	15	1	1	2	1	2	1	1	1	0	0	0	0	0	0	0	10
Cold Female	4	3	4	1	0	0	2	1	0	0	1	0	1	0	0	17	1	1	2	2	1	1	1	1	0	0	0	0	0	0	0	10
Cold Male	4	5	3	0	0	0	0	0	0	0	0	0	0	0	1	13	1	1	1	1	2	1	0	1	1	0	0	0	1	0	0	10
Age 0-10 All	2	0	0	0	0	1	0	0	0	0	1	0	0	0	0	4	5	5	5	8	6	6	3	3	3	6	6	5	5	5	5	76
Age 0-10 Female	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1	4	5	4	5	7	3	6	3	2	5	5	6	2	1	3	3	60
Age 0-10 Male	0	1	0	0	0	6	0	0	0	0	1	1	0	0	0	9	5	5	5	8	6	5	3	2	4	4	4	5	5	4	5	70
Age 11-60 All	3	3	0	0	0	0	0	0	0	0	0	0	0	0	0	6	3	3	2	3	5	2	0	1	2	3	3	0	3	3	3	36
Age 11-60 Female	1	3	0	0	1	0	0	1	0	0	1	0	0	0	0	7	2	3	2	2	5	1	0	1	1	3	3	0	2	5	5	35
Age 11-60 Male	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5	2	1	4	2	3	2	1	2	2	2	2	0	4	2	0	29
Age 60+All	4	5	4	3	3	0	0	1	3	2	0	0	0	0	0	25	1	3	2	5	6	3	1	1	1	1	0	0	0	3	2	29
Age 60+ Female	3	0	3	2	5	6	1	1	5	1	0	0	2	1	0	30	1	2	1	2	4	3	0	1	1	1	0	0	0	1	2	19
Age 60+ Male	4	4	0	0	0	0	0	0	0	0	0	0	0	0	0	8	1	1	4	7	5	2	1	2	0	0	0	0	0	1	0	24
Total	59	49	33	10	18	29	8	18	22	6	5	6	13	14	4	294	64	68	71	90	91	70	43	47	55	57	54	35	53	63	58	919

Figure 2 Total counts of positive statistically significant associations between pollution and ED visits by the considered stratum and lag (left: Circulatory, right: Respiratory).

Figure 3 plays a similar role, but it summarizes Figure 1 by statistically significant models between a pollutant and every lag considered. These two figures indicate that lags 0 and 1, lags 3 and 4, saw the most positive significant association for circulatory and respiratory, respectively. The strata most affected are “cold all” and “cold female, “age 0-10 all” and “age 0-10 male” for circulatory and respiratory cases, respectively.

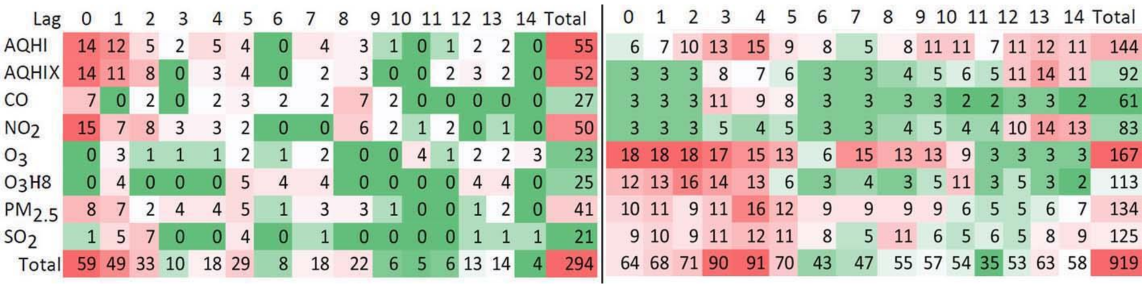


Air Pollution:	AQHI	AQHIX	CO	NO2	O3	O3H8	PM2.5	SO2	Total
All	3	3	2	4	0	0	2	2	16
Female	5	4	1	2	0	5	0	1	18
Male	2	2	1	2	0	0	2	1	10
Warm All	7	6	6	4	4	4	7	1	39
Warm Female	8	9	7	9	5	5	7	1	51
Warm Male	2	1	2	2	3	0	6	1	17
Cold All	3	3	0	3	1	1	2	2	15
Cold Female	3	3	0	4	2	2	1	2	17
Cold Male	2	3	0	3	1	0	2	2	13
Age 0-10 All	1	0	0	0	2	0	1	0	4
Age 0-10 Female	1	0	0	0	0	0	0	3	4
Age 0-10 Male	1	2	0	0	3	1	1	1	9
Age 11-60 All	2	2	0	1	0	1	0	0	6
Age 11-60 Female	1	1	0	1	2	2	0	0	7
Age 11-60 Male	1	1	1	1	0	0	1	0	5
Age 60+All	6	4	2	7	0	0	4	2	25
Age 60+ Female	5	6	4	5	0	4	4	2	30
Age 60+ Male	2	2	1	2	0	0	1	0	8
Total	55	52	27	50	23	25	41	21	294

Air Pollution:	AQHI	AQHIX	CO	NO2	O3	O3H8	PM2.5	SO2	Total
All	12	4	3	3	10	6	10	10	58
Female	8	3	0	2	9	6	8	8	44
Male	13	4	3	3	10	7	9	10	59
Warm All	15	15	15	15	15	15	15	15	120
Warm Female	15	15	15	15	14	15	15	12	116
Warm Male	15	15	12	13	15	14	15	15	114
Cold All	0	0	0	0	8	1	1	0	10
Cold Female	0	0	0	0	8	2	0	0	10
Cold Male	0	0	0	1	8	0	1	0	10
Age 0-10 All	15	9	2	8	6	6	15	15	76
Age 0-10 Female	12	6	2	6	4	5	11	14	60
Age 0-10 Male	15	8	2	6	6	5	15	13	70
Age 11-60 All	7	3	2	3	10	6	4	1	36
Age 11-60 Female	6	3	0	2	9	6	6	3	35
Age 11-60 Male	4	2	2	2	8	5	5	1	29
Age 60+All	3	2	1	2	10	5	2	4	29
Age 60+ Female	1	1	0	2	9	4	1	1	19
Age 60+ Male	3	2	2	0	8	5	1	3	24
Total	144	92	61	83	167	113	134	125	919

Figure 3 Total counts of statistically significant associations between pollution and ED visits by the considered stratum and pollutant or index (left: Circulatory, right: Respiratory).

Figure 4 summarizes the count of positive statistically significant associations between pollutants or indexes and ED visits for each considered lag. It shows that for circulatory cases, AQHI is a good metric of association as 55 out of the total 294 statistically significant positive associations between a pollutant or index and all strata were between AQHI and the lags, particularly in the first few lags (0-2). NO_2 has the highest amount of associations of the mono-pollutant models. For respiratory cases, O_3 is strongly associated with higher case frequency with a total of 167 associations. Similarly, to respiratory cases, the AQHI proves to be a good predictor of respiratory cases with a total of 144 associations.



Lag	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
AQHI	14	12	5	2	5	4	0	4	3	1	0	1	2	2	0	55
AQHIX	14	11	8	0	3	4	0	2	3	0	0	2	3	2	0	52
CO	7	0	2	0	2	3	2	2	7	2	0	0	0	0	0	27
NO_2	15	7	8	3	3	2	0	0	6	2	1	2	0	1	0	50
O_3	0	3	1	1	1	2	1	2	0	0	4	1	2	2	3	23
O_3H8	0	4	0	0	0	5	4	4	0	0	0	0	4	4	0	25
$PM_{2.5}$	8	7	2	4	4	5	1	3	3	1	0	0	1	2	0	41
SO_2	1	5	7	0	0	4	0	1	0	0	0	0	1	1	1	21
Total	59	49	33	10	18	29	8	18	22	6	5	6	13	14	4	294

Lag	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
AQHI	6	7	10	13	15	9	8	5	8	11	11	7	11	12	11	144
AQHIX	3	3	3	8	7	6	3	3	4	5	6	5	11	14	11	92
CO	3	3	3	11	9	8	3	3	3	3	2	2	3	3	2	61
NO_2	3	3	3	5	4	5	3	3	4	5	4	4	10	14	13	83
O_3	18	18	18	17	15	13	6	15	13	13	9	3	3	3	3	167
O_3H8	12	13	16	14	13	6	3	4	3	5	11	3	5	3	2	113
$PM_{2.5}$	10	11	9	11	16	12	9	9	9	9	6	5	5	6	7	134
SO_2	9	10	9	11	12	11	8	5	11	6	5	6	5	8	9	125
Total	64	68	71	90	91	70	43	47	55	57	54	35	53	63	58	919

Figure 4 Total counts of positive statistically significant associations between pollution and ED visits by the considered pollutant or index and lag (left: Circulatory, right: Respiratory).

The relative risk for lags 0, 1, 2 (circulatory) and 3, 4, 5 (respiratory) for pollutants shown to be particularly correlative was calculated and shown in Tables 4 and 5.

Table 4 Estimated RRs and their 95% confidence intervals (95% CI) for an increase of the AQHI value by a one interquartile range (IQR=1) for circulatory cases. Toronto, Canada, April 2004-December 2015.

Lags		**Lag 0**		**Lag 1**		**Lag 2**
Person/Age/Season	**RR**	**95%CI**	**RR**	**95%CI**	**RR**	**95%CI**
All	1.014	(1.008, 1.021)	1.011	(1.005, 1.017)	1.007	(1.001, 1.013)
Female	1.011	(1.003, 1.019)	1.011	(1.002, 1.019)	1.008	(1.000, 1.016)
Male	1.017	(1.009, 1.026)	1.011	(1.003, 1.020)	1.006	(0.998, 1.014)
Warm All	1.012	(1.006, 1.018)	1.009	(1.002, 1.015)	1.006	(1.000, 1.012)
Warm Female	1.007	(0.999, 1.015)	1.010	(1.002, 1.018)	1.006	(0.999, 1.014)
Warm Male	1.017	(1.009, 1.025)	1.008	(1.000, 1.016)	1.005	(0.997, 1.013)
Cold All	1.017	(1.010, 1.024)	1.014	(1.007, 1.021)	1.009	(1.002, 1.016)
Cold Female	1.016	(1.007, 1.025)	1.011	(1.002, 1.020)	1.010	(1.001, 1.019)
Cold Male	1.019	(1.010, 1.027)	1.017	(1.008, 1.026)	1.007	(0.998, 1.016)
Age 0-10 All	1.066	(1.003, 1.133)	1.019	(0.958, 1.083)	1.008	(0.947, 1.073)
Age 0-10 Female	1.065	(0.979, 1.160)	0.964	(0.883, 1.051)	1.052	(0.963, 1.149)
Age 0-10 Male	1.069	(0.993, 1.150)	1.053	(0.980, 1.133)	0.982	(0.911, 1.059)
Age 11-60 All	1.018	(1.008, 1.028)	1.012	(1.002, 1.022)	1.004	(0.994, 1.014)
Age 11-60 Female	1.012	(0.998, 1.026)	1.015	(1.001, 1.030)	1.009	(0.995, 1.023)
Age 11-60 Male	1.023	(1.010, 1.035)	1.010	(0.998, 1.023)	1.000	(0.988, 1.012)
Age 60+All	1.012	(1.004, 1.019)	1.010	(1.003, 1.017)	1.009	(1.001, 1.016)
Age 60+ Female	1.010	(1.001, 1.019)	1.009	(1.000, 1.018)	1.008	(0.998, 1.017)
Age 60+ Male	1.013	(1.004, 1.023)	1.012	(1.002, 1.022)	1.010	(1.000, 1.020)

Table 5 Estimated RRs and their 95% confidence intervals (95% CI) CIs for an increase of concentration of ozone (O_3) by a one interquartile range (IQR=12.8 ppb) for Respiratory cases. Toronto, Canada, April 2004-December 2015.

Lags		**Lag 3**		**Lag 4**		**Lag 5**
Person/Age/Season	**RR**	**95%CI**	**RR**	**95%CI**	**RR**	**95%CI**
All	1.033	(1.019, 1.101)	1.025	(1.011, 1.076)	1.017	(1.003, 1.052)
Female	1.042	(1.025, 1.128)	1.030	(1.014, 1.093)	1.016	(0.999, 1.047)
Male	1.025	(1.010, 1.076)	1.020	(1.005, 1.060)	1.019	(1.004, 1.057)
Warm All	1.019	(1.009, 1.056)	1.016	(1.007, 1.049)	1.014	(1.004, 1.041)
Warm Female	1.020	(1.009, 1.061)	1.015	(1.004, 1.046)	1.013	(1.001, 1.038)
Warm Male	1.017	(1.006, 1.052)	1.017	(1.006, 1.052)	1.014	(1.003, 1.043)
Cold All	1.052	(1.033, 1.161)	1.039	(1.020, 1.121)	1.027	(1.008, 1.082)
Cold Female	1.069	(1.047, 1.217)	1.051	(1.030, 1.158)	1.025	(1.004, 1.075)
Cold Male	1.035	(1.016, 1.107)	1.028	(1.009, 1.084)	1.029	(1.011, 1.090)
Age 0-10 All	1.035	(1.015, 1.108)	1.020	(1.000, 1.062)	1.005	(0.985, 1.014)
Age 0-10 Female	1.045	(1.019, 1.138)	1.024	(0.999, 1.073)	0.989	(0.964, 0.966)
Age 0-10 Male	1.029	(1.006, 1.087)	1.018	(0.996, 1.054)	1.016	(0.994, 1.049)
Age 11-60 All	1.029	(1.012, 1.087)	1.020	(1.004, 1.060)	1.017	(1.001, 1.051)

Age 11-60 Female	1.040	(1.021, 1.123)	1.023	(1.004, 1.068)	1.015	(0.996, 1.045)
Age 11-60 Male	1.017	(0.999, 1.050)	1.017	(0.999, 1.051)	1.019	(1.001, 1.057)
Age 60+All	1.041	(1.023, 1.125)	1.042	(1.023, 1.128)	1.032	(1.014, 1.099)
Age 60+ Female	1.042	(1.019, 1.130)	1.053	(1.030, 1.165)	1.041	(1.018, 1.126)
Age 60+ Male	1.039	(1.017, 1.120)	1.029	(1.007, 1.088)	1.023	(1.002, 1.070)

As mentioned earlier, for circulatory cases, the “cold all” and “cold female” strata were most affected at these lags. The relative risk for these strata at lags 0 and 1 was 1.017 and 1.012, 1.015 and 1.011, respectively. It is noted that the RR for ages 0 to 10 is very high, however this is due to the relatively small total case count. For respiratory cases, lags 3 and 4 were most significant, with “age 0-10 all” and “age 0-10 male” having the most associations among all strata. At lags 3 and 4, these strata had relative risks of 1.035 and 1.029, 1.020 and 1.018, respectively. The relative risks and their 95% confidence intervals were calculated for an increase of one IQR of air pollutant for all considered combinations of air pollutants, their lags, and strata. Their values are re-ported in the following files: CARDIACRRiskToronto.csv and RESPIRATORYRRiskToronto.csv, found in Supplementary Materials.

4. Discussion

Numerous studies have shown a strong correlation between elevated ambient air pollution levels and increased rates of mortality and morbidity associated with respiratory [17-19], and circulatory complications [6, 8, 19, 20]. It was therefore expected to find that there were many positive associations between certain strata and air pollutants. For respiratory disease-related cases, it was observed that lags 3 and 4 were most significant, thus acute responses to short-term air pollution exposure are highly likely compared to other lags. This observation is reflected by previous findings, as it has been shown by D’amato et al. [17] that ambient air pollution can significantly in-crease the risk of respiratory illness and aggravate pre-existing conditions in the short-term. Our results also showed a significant correlation between individuals aged 0-10 years and visits to the ED. This association has been observed in many studies [10, 21, 22], which have highlighted increases in emergency department visits related to respiratory illness among children (aged 5-9 years) related to short-term exposure to air pollution [22]. Our results follow the findings of Alhanti et al. [23], that the highest for asthma-related (most common chronic respiratory illness in Canada according to Statistics Canada) ED visits concerned the 5 to 18 year age group. Our results showed that out of all individual pollutants, the highest count of positive associations for respiratory cases was found to be with O_3. Ozone has been shown to be a significant factor in worsening of respiratory conditions [19], however we report few associations between O_3 and the most affected strata, children 0-10. While ozone has elevated counts of positive associations with all other strata relatively to some other pollutants, the 0-10 age group irrespective of sex is uniquely affected by $PM_{2.5}$ and SO_2 levels. A possible explanation to this observation is that children spend less time out-side on hotter days, when O_3 levels are elevated due to elevated temperature.

As with respiratory illnesses, air pollution is also known to have a detrimental effect on the circulatory system [19, 20]. This is especially the case for particulate matter ($PM_{2.5}$) [19, 24] and NO_2, [19, 25] corresponding to the two highest mono-pollutant positive association counts in this study (34 and 45 respectively). ED visits related to circulatory problems saw positive associations at the shortest lags (0 and 1 days in particular), consistent with previous findings [19]. It has been shown that in early lags, exposure to NO_2 can increase circulatory inflammation by triggering an elevated level of high-sensitivity C-reactive protein [26]. Our results also show that adverse circulatory response is aggravated in the cold months, a relationship which has been demonstrated previously [27]. In colder months, ambient air pollution levels are relatively high, contributing to elevated risk for individuals with pre-existing cardiovascular conditions.

Some associations were negative (shown in Supplementary Materials), implying there is an inverse relationship between increasing levels of air pollution and ED visits for particular strata and pollutants. It is possible that these negative correlations are due to people being aware of reports of elevated AQHI or other pollutant values for a particular day, and avoid exposing themselves to urban environments where the pollution levels are highest. It is of note that the most negative correlations occur for NO_2, seen in Figure e2 (see in Supplementary Materials) for respiratory conditions. The strata/lag combinations with negative associations almost all correspond to strata/lag combinations for AQHI with null associations (nitrogen dioxide is one of the pollutant factors in the AQHI formula). This could in part explain why there were very few positive NO_2 associations in the short-term, even though NO_2 has been shown to increase mortality and morbidity rates in this period [28]. While the short-term effect of NO_2 on respiratory ED visits was inverse, it was shown that in the longer term (lags 12-14) NO_2 was the only mono-pollutant with significant increases in ED visit totals. It is possible that the accumulation of NO_2 in the lungs through repeated exposure can lead to delayed respiratory effects, as NO_2 is not very water soluble, and therefore does not produce irritation immediately in the upper respiratory tracts but rather deeper into the bronchi [29, 30].

To compensate for the high amount of statistical associations being made and thus limit the impact of the multiple comparison problem on inferences made in this paper, a “persistence test” was performed. Index and lag, or strata and lag combinations which had the highest totals of statistically significant positive associations at p-value 0.05 in majority remained statistically significant when a more stringent p-value ($p<0.001$) was applied. Visits to the ED in the 0-10 age group for respiratory problems remained strongly associated to levels of $PM_{2.5}$ and SO_2, as did O_3 for almost all strata. For circulatory cases, NO_2 remained strongly associated with most strata at lag 0, while $PM_{2.5}$ did not.

Given these results and concurrence with available literature, it is reasonable to validate the hypothesis proposed in this study.

The primary limitation of this work is that it does not control for exposure duration, thus it assumes similar exposure for all tracked cases. We also acknowledge that this study does not control for heterogeneity of exposure to air pollution in a population. Individuals may be affected by numerous sources of pollution that may not be registered by an ambient air pollution monitor, such as their proximity to traffic [31-33]. Other sources of exposures which affect human health are cooking emissions [34-36], power plants emissions [37], wildfires [38], and air pollutants generated from active and passive tobacco smoke [39].

Finally, the multiplicity of comparisons performed in this study introduces a possibility of erroneous associations and thus misguided inferences. To combat this, the same analysis using a much more stringent p-value than the original $p=0.05$ was contrasted against the latter, and the results showed a persistence of the combinations of strata, lags and pollutants that showed the most statistically significant associations in the primary analysis.

5. Conclusions

This study's objective was to shed light on how fluctuations of air pollution levels affect cardiovascular and respiratory related ED visits with respect to patient age, sex, seasonality, and lag. We have demonstrated that exposure to elevated ambient air pollution levels, particularly NO_2 and O_3, are positively associated with the number of ED visits related to circulatory and respiratory cases. These correlations were strongest at 0, 1 and 3, 4 days post-exposure for circulatory and respiratory illnesses, respectively. It was also reinforced that the common air pollution indicator AQHI is a good multi-pollutant predictor of elevated circulatory and respiratory cases at the specified lags. These conclusions were mostly upheld when using a more stringent p-value.

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Additional Materials

The following additional materials (Supplementary Materials) are uploaded at the location https://github.com/szyszkowiczm/CardioRespirTORONTO. CARDIACRRiskToronto.csv - contains the estimated relative risks for all models (2160) for ED visits for cardiac problems. CARDIACToronto.csv - contains the estimated slopes and their standard errors for all models (2160) for ED visits for cardiac problems. Figure e1 (Cardiac).jpg- a map of the associations for cardiac problems. Figure e2 (Respiratory).jpg - a map of the associations for respiratory problems. Figure e3 (RR, Cardiac, NO2).jpg - forest plot for cardiac and NO2. Figure e4 (RR, Respiratory, O3).jpg - forest plot for respiratory and O3. HistAQHI-AQHIX-CO-NO2.jpg - histogram of AQHI, AQHIX, CO, and NO2. HistO3-O3H8-PM25-SO2.jpg - histogram of O3, O3h8, PM2.5, and SO2. HistTempRHum.jpg -histogram of temperature and relative humidity. RESPIRATORYRRiskToronto.csv - contains the estimated relative risks for all models (2160) for ED visits for respiratory problems. RESPIRATORYToronto.csv - contains the estimated slopes and their standard errors for all models (2160) for ED visits for respiratory problems. TorontoMapStation.jpg - map of Toronto: station locations and population density.

Author Contributions

Mieczysław Szyszkowicz: Conceptualization, Data Curation, Methodology, Software, Supervision, Formal analysis, Writing-original draft, Writing-review & editing, Project administration; Nicholas de Angelis: Formal analysis, Methodology, Validation, Visualization; Writing-review & editing.

Competing Interests

The authors have declared that no competing interests exist.

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