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Urban air pollution and emergency department visits for influenza

Abstract

Introduction. There is a large body of research which suggests that air pollutants might affect infectious diseases, their transmission, severity, and a length of recovery.

Aim. The aim of this study is to examine the relationships between ambient air pollution and emergency department (ED) visits for influenza and viral pneumonia in Toronto, Canada.

Material and Methods. The National Ambulatory Care Reporting System database was used to drawn ED visits (4 282 days). Five ambient air pollutants: carbon monoxide, nitrogen dioxide, sulphur dioxide, ozone (CO, NO_2, SO_2, O_3, O_3H_8 – ozone as a maximum eight hour average, respectively), and fine particulate matter ($PM_{2.5}$) were examined. In addition, the Air Quality Health Index (AQHI; combines NO_2, O_3, and $PM_{2.5}$) was tested. Conditional Poisson models were constructed using daily counts of ED visits. Temperature and relative humidity in the models were represented by natural splines. Air pollutants and weather factors were lagged by 0 to 14 days. The analysis was done by strata of age group, sex, and two seasons.

Results. In the period of the study, 26,200 ED visits were identified; 13,963 for females and 12,237 for males. For each air pollutant, 270 models were generated (18 strata x 15 lags). Ambient air pollution concentrations lagged by 10 and 11 days have the highest impact on ED visits, with 48 and 47 positive associations, respectively. Ozone has 181, sulphur dioxide has 104, and $PM_{2.5}$ has 76 among the 417 total positive statistically significant (P-Value<0.05) associations. For all persons an increase (12.8 ppb) in ambient ozone lagged by 0, 1, and 2 days gives the following relative risks and their 95% confidence intervals 1.214 (1.135, 1.299), 1.200 (1.121, 1.284), and 1.179 (1.102, 1.263), respectively.

Conclusion. The results suggest that exposures to urban ambient air pollution affect the number of ED visits for viral respiratory illness.

Keywords: age; air pollution; case-crossover; concentration; counts; Poisson; strata; urban.

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INTRODUCTION

The relationship between elevated air pollution concentrations and increased number of emergency department (ED) visits, morbidity, and mortality is well established in the literature related to environmental epidemiology [1-3]. In recent years, we have witnessed the expansion of the literary body on the correlation between air pollution and various health effects from respiratory and cardiac conditions to diseases belonging to categories such as metabolic, infective, cognitive, psychological [3,4]. There does exist, however, a wide spectrum of associations that remain unexplored. The present pandemic of SARS-CoV-2 is an opportunity to test associations between air pollution and influenza cases, which could potentially be analogous to the interaction between air pollutants and SARS-CoV-2. Literature on the effect of air pollution on the behavior of influenza infections is substantial; hence associations observed in this study may be supported by previously established biological processes.

AIM

The primary aim of this study is to investigate the hypothesis that there is a correlation between ambient air pollution concentration levels and emergency department (ED) visits for influenza and viral pneumonia.

Our hypothesis is based on the principle that air pollution may have an immunosuppressive effect on the body's defenses [5,6]. It is thus reasonable to expect associations between elevated air pollution levels and higher ED visit frequencies for influenza and viral pneumonia. While we cannot directly contrast associations between air pollution and influenza ED visits with those of SARS-CoV-2, these viruses share numerous similarities [7], which suggests that the results obtained in this study may carry over to associations observed between the SARS virus and air pollution concentrations.

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MATERIAL AND METHODS

Health data

The analyzed data were drawn from the National Ambulatory Care Reporting System database (NACRS 2020, [8]) for a period of 4,292 days (April, 2004 – December, 2015). The NACRS database organizes health data for all hospital-based and community-based ambulatory care, including records on emergency department (ED) visits. ED visits were filtered only by the primary cause classification of the visit, and extracted from the NACRS database if classified under ICD-10 codes J09-J12 (influenza and viral pneumonia). The geographical area of this study is the Census Division (CD) of Toronto, Ontario, Canada. The population studied were individuals registered in ED with home addresses located in the area determined by the CD of Toronto, an area with a population of 2,731,571 people in 2016. The resulting population density of this region is an estimated 4,334.4 people per square kilometer. The retrieved cases were organized as daily counts. The applied statistical models use these counts as the investigated health outcomes. As a time unit – one day is used.

Environmental data

The air pollution data were obtained from the National Air Pollution Surveillance (NAPS), maintained by Environment and Climate Change Canada (NAPS 2020, [9]). Hourly data from seven air pollution monitoring stations were averaged over one day to estimate air pollution concentration levels for the whole area. Daily values of air pollutants and weather conditions were organized as one dataset and linked with daily ED visits counts. This dataset (air pollution and weather) has already been used in other studies related to ambient air pollution exposure to assess short term mortality risks and excess mortality in Toronto [10,11].

Five urban ambient air pollutants were investigated in the statistical models: carbon monoxide (CO), nitrogen dioxide (NO_2), ground-level ozone (O_3 – as a daily average, O_3H_8 – as a maximum eight hour average), fine particulate matter ($PM_{2.5}$), and sulphur dioxide (SO_2).

In addition to these five air pollutants, we examined the Air Quality Health Index (AQHI), an index constructed using three individual ambient air pollutants (O_3, NO_2, and $PM_{2.5}$). The index values incorporate air pollutant concentration levels and the health risk estimations determined by mortality rates in large Canadian cities [12]. AQHI values are published in Canada as integer numbers on a scale (1-10, 10+) to represent the risk related to ambient air quality. In this study however, continuous values of the AQHI are used. The values were calculated according to the formula [12].

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

Additionally, another form of the index, here referred to as the AQHIX, was calculated using O_3H_8 concentration levels rather than ozone (O_3) where, instead of a daily average, an average of the peak 8 hours of ozone pollution is used. The AQHIX emphasizes the presence of ozone among its three air pollutant components more than the AQHI.

Statistical model

The case-crossover schema applied in this study is designed to control for all measured and unmeasured time-invariant confounders, including smoking, socioeconomic position, and comorbidity [13]. In the constructed models, temperature and relative humidity were incorporated in the form of natural splines with three degrees of freedom. The time-stratified approach was used to group the data by the same weekday in a common month [14]. The statistical model outputs were the coefficients (Beta) related to air pollutants and their standard errors (SE-Beta). Using these values (Beta, SEBeta), relative risks (RR) could be easily determined for an increase in the concentration levels by taking the exponential of the product of a one interquartile range (IQR) and Beta (RR=exp(Beta*IQR)). The statistical calculations were done using conditional quasi-Poisson regression models [15-20]. Given the relatively short incubation period of both SARS-CoV-2 and influenza, this study uses one day as the time unit. The calculations were performed in R statistical software using the gnm procedure (generalized nonlinear models) with the "quasipoisson" option enabled (R Core Team, 2018; [21]). In total, 2,160 statistical models (15 lags x 18 strata x 8 – air pollutants or index values) were constructed. The realized statistical models have the following form

ModelFLU = gnm(EDFLU~APollutant + ns(Temperature,3) + ns(RelativeHumidity,3)),

where the options data=EDVisitsFLU, family=quasipoisson, eliminate=factor(Cluster) were added. EDFLU represent daily counts for the considering strata. The quasi-Poisson is used to model an overdispersed count variable. Here Cluster represents a group (4 or 5) of days of the same weekday in a common month and the Cluster has the hierarchical-calendar driven structure <year:month:weekday>.

The results from all models are listed in Supplementary Materials. A p-value <0.05 was considered statistically significant, however, given the multiple comparison limitation, statistical significance was also evaluated using the more stringent criterion of p-value <0.001.

Ethics

The Health Canada Research Ethic Board determined that the study is IRB exempt, given that patient data were pre-existing and de-identified.

RESULTS

The results are based on ED visits identified using ICD-10 codes J09–J12 (covering influenza and viral pneumonia; Influenza due to certain identified influenza virus, Influenza due to other identified influenza virus, Influenza with pneumonia, other influenza virus identified, Influenza, virus not identified, and Viral pneumonia, not elsewhere classified). In the studied period, 26,200 such ED meeting the inclusion criteria visits were identified, of which 13,963 were female patients and 12,237 were male patients. Table 1. shows the statistics on the daily counts of ED visits for all 18 strata. In the warm months (April-September), there were 12,333 visits and in the cold months (October-March) there were 13,867 ED visits.

TABLE 1. Statistics on ED visits for influenza, ICD-10 codes: J09 – J12. Toronto, Canada, April, 2004 – December, 2015.

Strata/Factors	ED visits	Min	Q1	Median	Mean	Q3	Max
All	26,200	0	1	2	6.1	5	368
Female	13,963	0	0	1	3.3	3	184
Male	12,237	0	0	1	2.9	3	184
Warm All	12,333	0	0	1	5.2	4	368
Warm Female	6,308	0	0	1	2.7	2	184
Warm Male	6,025	0	0	1	2.5	2	184
Cold All	13,867	0	2	4	7.2	8	85
Cold Female	7,655	0	1	2	4.0	4	55
Cold Male	6,212	0	1	2	3.2	4	40
Age 0-10 All	4,983	0	0	0	1.2	1	154
Age 0-10 Female	2,171	0	0	0	0.5	0	68
Age 0-10 Male	2,812	0	0	0	0.7	0	86
Age 11-60 All	17,967	0	0	2	4.2	4	202
Age 11-60 Female	9,810	0	0	1	2.3	2	107
Age 11-60 Male	8,157	0	0	1	1.9	2	95
Age 60+All	3,250	0	0	0	0.8	1	28
Age 60+ Female	1,982	0	0	0	0.5	0	19
Age 60+ Male	1,268	0	0	0	0.3	0	13
PM2.5	µg/m3	0.1	4.7	7.1	8.9	11.2	65.5
NO2	ppb	3.2	11.1	15.0	16.1	19.9	59.8
O3	ppb	1.7	16.8	23.0	23.5	29.6	62.1
O3H8	ppb	9.0	33.0	41.0	43.7	52.0	107.0
SO2	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	oC	-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: The column labelled as "ED visits" shows the number of ED visits and the used units for environmental factors, Min – minimum, Max –maximum, Q1-25th percentile, Q3-75th percentile.

Persons under the age of 11 accounted for 4,983 visits, 17,967 were persons between 11 and 60 years of age, and finally those older than 60 counted for 3,250 visits. Table 1. also summarizes the statistics on ambient air pollutants, temperature, and relative humidity for the period of the study.

Figures 1, 2, and 3 show the frequencies of positive statistically significant associations (value of the coefficient Beta is positive) obtained for the corresponding specifications (stratum, air pollutant, lag) given in a row and column. The cells show the total number of such associations. For example, in Figure 1, in the row identified as "All" and a column identified as "lag 0", the value provided in the cell (here 2) with such coordinates indicates the total number of positive associations for any of the considered air pollutants. The colors in Figures 1-3. are applied to distinguish and highlight the patterns of associations. There were a total 417 positive statistically significant associations (using a p-value<0.05) among all pollutants and for all lags and strata. When applying a more stringent p-value criterion (<0.001) we observed 215 positive and statistically significant associations. Thus 52% of the positive statistically significant associations persisted under a more demanding criterion. While there were many negative associations for AQHI, AQHIX, CO and NO2, none of them remained significant when applying a p-value<0.001.

Figure 1 is organized with the 18 strata in rows and 15 lags (0-14 days) in columns, thus summarizing the counts of positive statistically significant associations for all pollutants at all strata and lags. Lags of 10 and 11 days saw the highest total number of positive associations at 48 and 47 respectively, among the grand total of 417.

Lag	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
All	2	2	2	1	1	1	2	2	2	3	4	4	2	1	0	29
Female	2	1	2	1	1	1	2	2	2	3	4	3	1	1	0	26
Male	1	2	2	1	1	1	2	1	1	3	3	4	2	1	0	25
Warm All	0	1	2	1	1	2	2	2	3	4	5	5	3	3	2	36
Warm Female	1	1	1	0	0	3	1	2	3	4	4	4	2	3	2	31
Warm Male	0	1	2	1	1	2	2	2	2	5	5	5	3	1	3	35
Cold All	2	2	2	2	1	1	1	2	0	0	0	0	0	0	0	13
Cold Female	2	1	2	2	1	1	1	2	1	0	0	0	0	0	0	13
Cold Male	1	2	2	2	1	1	2	1	0	0	0	0	0	0	0	12
Age 0-10 All	1	2	2	2	0	1	1	2	1	3	5	5	3	2	2	32
Age 0-10 Female	2	2	1	1	0	0	0	1	1	2	5	4	2	3	2	26
Age 0-10 Male	1	2	2	0	0	1	1	2	1	4	5	5	4	1	1	30
Age 11-60 All	1	1	2	1	1	2	2	2	3	3	4	4	1	1	1	29
Age 11-60 Female	1	1	2	1	1	2	2	2	3	3	4	3	1	1	0	27
Age 11-60 Male	1	2	2	1	1	1	2	1	1	2	0	0	1	1	0	16
Age 60+All	3	1	2	1	1	1	1	1	1	0	0	0	0	0	0	12
Age 60+ Female	2	2	1	1	1	1	1	1	0	1	0	1	0	0	0	12
Age 60+ Male	2	1	2	2	1	1	2	1	1	0	0	0	0	0	0	13
Total	25	27	33	21	14	23	27	29	26	40	48	47	25	19	13	417

FIGURE 1. All pollutants combined. Frequencies of positive associations: strata (rows), lags (columns). Toronto, Canada. 2004-2015.

Figure 2. again summarizes total positive associations, however, it does so by the 8 air pollutants and indexes in rows and the 15 lags in columns. It reveals a stark separation between pollutants or indexes, with AQHI, AQHIX, CO and NO_2 accounting for only 16 associations, while the remaining pollutants account for 401. Of the latter total, ozone (O_3) accounts for 181 of the observed associations.

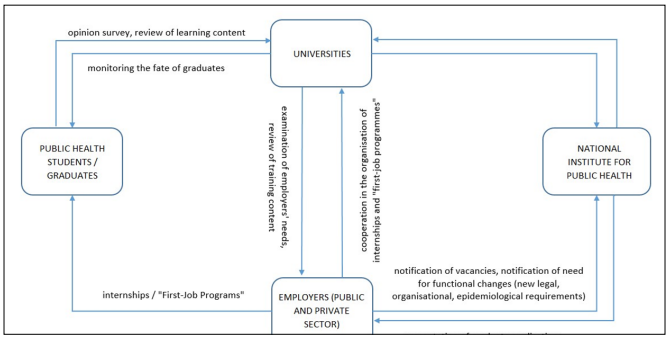

FIGURE 2. All strata combined. Frequencies of positive associations: air pollutants (rows), lags (columns). Toronto, Canada. 2004-2015.

Figure 3 summarizes the results by all lags, with 18 strata and the 8 air pollutants or indexes in its rows and columns, respectively. The highest total of significant positive associations corresponded to the 'Warm All' stratum, accounting for all genders and age groups during the warmer months, with 36 observed associations.

Air Pollution:	AQHI	CO	NO2	O3	H8	PM2.5	SO2	Total
All	0	0	0	12	2	5	10	29
Female	0	0	0	12	1	5	8	26
Male	0	0	0	12	1	5	7	25
Warm All	3	0	0	9	3	10	11	36
Warm Female	0	0	0	8	3	8	12	31
Warm Male	5	0	0	8	3	10	9	35
Cold All	0	0	0	8	4	0	1	13
Cold Female	0	0	0	9	3	0	1	13
Cold Male	0	0	0	8	3	0	1	12
Age 0-10 All	3	0	0	12	2	6	9	32
Age 0-10 Female	1	0	0	11	3	5	6	26
Age 0-10 Male	4	0	0	10	3	6	7	30
Age 11-60 All	0	0	0	12	2	7	8	29
Age 11-60 Female	0	0	0	12	1	6	8	27
Age 11-60 Male	0	0	0	10	0	3	3	16
Age 60+All	0	0	0	9	2	0	1	12
Age 60+ Female	0	0	0	10	2	0	0	12
Age 60+ Male	0	0	0	9	2	0	2	13
Total	16	0	0	181	40	76	104	417

FIGURE 3. All lags combined. Frequencies of positive associations: strata (rows), air pollutants (columns). Toronto, Canada. 2004-2015.

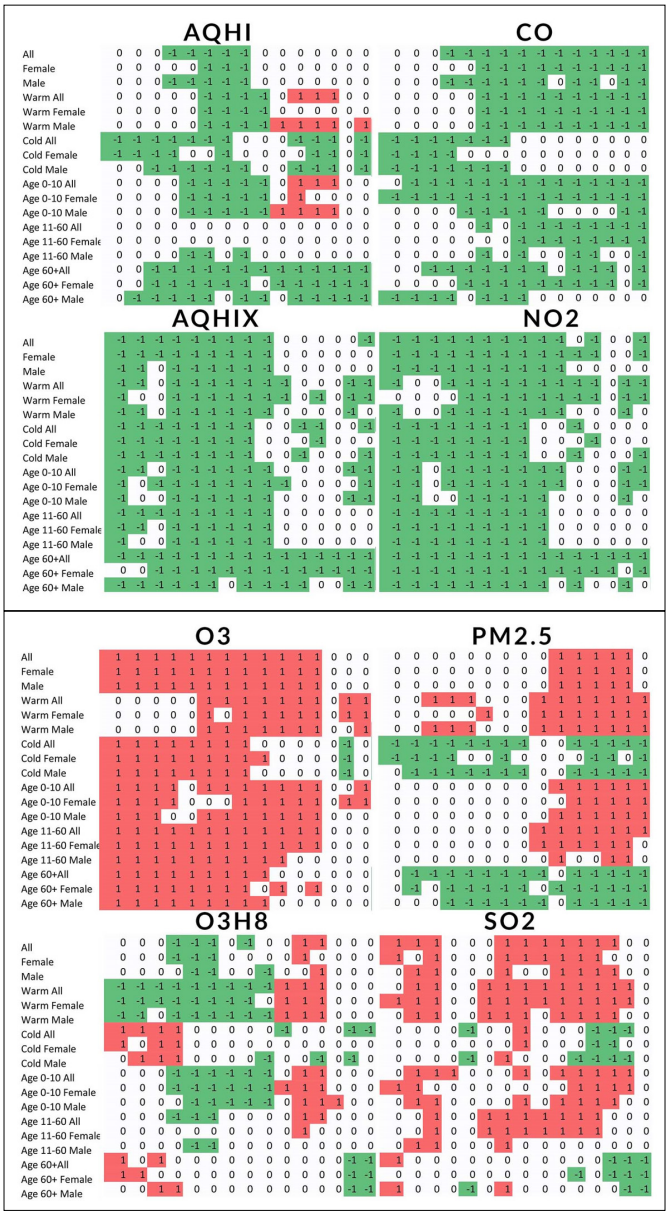

FIGURE 4A and 4B. A map to numerical results; strata (rows), lags (columns). 0/white – no associations, and statistically significant: -1/green – negative, 1/red – positive. The results are grouped by air pollutants. Toronto, Canada. 2004-2015. 2004-2015.

Figures 4a and 4b represent a visualization of every individual model significance result per combination of stratum, lag and pollutant. The associations are classified as statistically significant positive (represented with a 1), negative (-1) or no significant association (0). Colours are used to aid the visualization of these relationships (red, green, and white, respectively). The columns represent lags from 0 to 14 days. The corresponding numerical values of coefficients β and its standard error are available as Supplementary Materials.

As the number of models is large, the relative risk is only shown for a particular pollutant and lags at all strata. The remaining numerical results are given in Supplementary Materials. Ambient ozone shows the highest number of positive associations among the considered air pollutants and indexes,

TABLE 2. Estimated RRs and their 95% confidence intervals (95% CI) CIs for an increase of concentration of ozone (O3) by one interquartile range (IQR=12.8 ppb) for Respiratory 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	1.214	(1.135, 1.299)	1.2	(1.121, 1.284)	1.179	(1.102, 1.263)
Female	1.206	(1.120, 1.298)	1.206	(1.120, 1.299)	1.169	(1.085, 1.259)
Male	1.223	(1.131, 1.323)	1.192	(1.103, 1.289)	1.191	(1.101, 1.288)
Warm All	1.064	(0.980, 1.155)	1.055	(0.970, 1.147)	1.057	(0.970, 1.153)
Warm Female	1.057	(0.968, 1.154)	1.059	(0.967, 1.160)	1.031	(0.939, 1.132)
Warm Male	1.072	(0.976, 1.177)	1.051	(0.957, 1.153)	1.084	(0.984, 1.193)
Cold All	1.294	(1.223, 1.368)	1.286	(1.217, 1.360)	1.26	(1.193, 1.331)
Cold Female	1.284	(1.205, 1.367)	1.288	(1.210, 1.371)	1.253	(1.178, 1.333)
Cold Male	1.307	(1.223, 1.396)	1.285	(1.203, 1.371)	1.269	(1.189, 1.353)
Age 0-10 All	1.258	(1.124, 1.408)	1.234	(1.103, 1.381)	1.202	(1.075, 1.344)
Age 0-10 Female	1.322	(1.164, 1.501)	1.222	(1.076, 1.388)	1.138	(1.004, 1.291)
Age 0-10 Male	1.214	(1.072, 1.375)	1.244	(1.101, 1.406)	1.254	(1.109, 1.417)
Age 11-60 All	1.176	(1.098, 1.259)	1.163	(1.085, 1.245)	1.161	(1.083, 1.244)
Age 11-60 Female	1.149	(1.063, 1.241)	1.168	(1.080, 1.262)	1.161	(1.074, 1.256)
Age 11-60 Male	1.208	(1.113, 1.311)	1.156	(1.066, 1.254)	1.16	(1.069, 1.258)
Age 60+All	1.367	(1.239, 1.510)	1.355	(1.229, 1.494)	1.251	(1.135, 1.380)
Age 60+ Female	1.404	(1.258, 1.566)	1.388	(1.245, 1.548)	1.247	(1.119, 1.390)

thus it is here illustrated. An increase in O_3 concentration by one IQR (12.8 ppb) are shown in Table 2, along with the 95% confidence intervals.

SUPPLEMENTARY MATERIALS

The corresponding files are located at https://github.com/szyszkowiczm/TorontoFLU. These files are FLUToronto.csv (contains Beta and its standard error for 2,160 models), FLUTorontoAll.jpg (Figure 4.), FLUTorontoRRisk.csv (calculated relative risks for a one IQR increase), HistAQHI-AQHIX-CO-NO2.jpg, HistO3-O3H8-PM25-SO2.jpg, HistTempRHum.jpg (these 3 files contain histograms), TorontoMapStation2015.jpg (contains Toronto's map).

DISCUSSION

The results obtained in this study demonstrate that certain air pollutants and the number of ED visits for influenza and viral pneumonia-related symptoms are positively associated. As seen in Figure 2, there is a strong division between pollutants, with O_3, SO_2 and $PM_{2.5}$ being more consistently associated with ED visits for influenza, while the AQHI, AQHIX, NO_2 and CO exhibited few significant associations with ED visits. Given its adverse effect on the respiratory system, when contrasting our results with existing literature, it is surprising that NO_2 was found to have no positive statistically significant correlation [5,22-26]. Ozone, however, was shown to have the greatest number of significant positive associations at lags up to 11 days, and for a majority of strata. Given its strongly oxidative properties and evidence provided in this paper, it may be suggested that ozone is a strong moderator of viral infection in a population. When applying a more stringent p-value to determine the number of significant associations, O_3 saw 70% of associations remained significant. An interesting characteristic of ozone and its associations by strata and lags is the lack of association for early lags in the warm months when the strata are adjusted for seasonality. Cold weather has been shown to induce an increase in respiratory infections [27], thus the associations between lags 0 and 8 are expected. Intriguingly, all statistically significant positive associations (even at $p<0.001$) for warm weather strata are located after a lag of 5 days for a less constrained p-value, and after 9 days lag for $p<0.001$. This may suggest that warmer weather delays development of influenza symptoms, thus delaying an ED visit from initial exposure.

$PM_{2.5}$ also showed a high remainder of positive associations of 49% under a more stringent p-value. However, the associations were not as homogenous as it was observed with O3; rather, most associations were seen for lags 9 to 14, and showed negative statistically significant correlation for "cold" period strata as well as the oldest age group (60+) at $p<0.05$. At a stringent p-value, the most affected strata were children aged 0-10, as well as the "warm" period strata, both irrespective of gender. $PM_{2.5}$ poses a danger to the respiratory system as smaller particles can penetrate much deeper into the lungs than PM_{10} or larger. Given their small size but large surface area, $PM_{2.5}$ can act as a transport for viruses deep into the lungs [28].

While it did not show the same level of persistence as O_3 or $PM_{2.5}$, nevertheless SO_2 had the second highest total of associations at 107. Again concentrated at the later lags, particularly 10-13 days, SO_2 proved to have similar patterns of associations as $PM_{2.5}$. The "cold" period strata and age 60+ strata both saw few associations at $p<0.05$, and only 2 at $p<0.001$. Given that cold weather typically sees higher levels of air pollution and a higher likelihood of respiratory infection, this pattern for both $PM_{2.5}$ and SO_2 is curious.

Given the provided evidence that air pollutants negatively affect lung immunity and viral resistance, it is justifiable to say that the results obtained in this study are reasonable.

The results found in this study may be important to consider in the context of the ongoing SARS-CoV-2 pandemic. During the emergence of the SARS-CoV-2 pandemic (colloquially known as COVID-19), many medical institutions braced for a large influx of new patients. As emergency departments are at the front line of new patient admissions, they are particularly impacted by an increase in cases. While the current SARS-CoV-2 pandemic provoked a surge of new research in domains of virology, medicine and epidemiology, it is very difficult to study the impact of air pollution on the interaction between the virus and large populations. Given the nature of this study and the data required to perform it, it will be impossible to create accurate statistical models at present, illustrating how respiratory infection emergency department visits are associated with air pollution levels. Hence, to study the impact of air pollution on how a virus such as SARS-CoV-2 affects ED visits, we turn to very common respiratory infections – influenza infections.

There are, of course, differences between the two viruses which the authors acknowledge, but in the scope of this study, moderate differences in infection pathways could potentially be disregarded. The viruses are classified in different Baltimore virus classes, but the pathways of cell infection are similar. SARS-CoV-2 is a (+)ssRNA virus, while influenza is a (-)ssRNA virus, both share an enveloped capsid with helical symmetry. Both viruses have similar incubation periods, where influenza infections present symptoms within 1-4 days of exposure [29], while SARS-CoV-2 (along with other SARS coronaviruses) has been shown to present symptoms within 5 days post-exposure in the majority of cases [29,30]. Both viruses can be transmitted via droplets, surface contact and have been shown to be airborne [31-35]. These similarities in virus structure and incubation period may warrant the assumption that both viruses will capitalize on respiratory tracts affected by air pollution in similar ways. Thus, interpretation of our results for the influenza virus may carry over to SARS-CoV-2.

Differences are to be expected between influenza and COVID-19 when comparing ED visit numbers for different strata, however, elderly individuals infected with SARS-CoV-2 present symptoms at a higher rate than younger individuals [32,36], while influenza is seen more commonly in the latter [37]. It is, therefore, necessary to contrast our results to evidence that air pollutants can facilitate viral infection in the respiratory tract. Literature provides clear indication of how pathways created by various pollutants affect viral infection. Exposure to the majority of individual pollutants examined in this study has been linked to lower immunological viral resistance, ease of reinfection, and overall worse health outcomes. The primary mechanisms by which air pollutants weaken the immune system are oxidative stress [5,38,39], macrophage inactivation, and reduced expression of hydrophilic surface proteins [5,38,40]. All these mechanisms contribute to a weakened immune system, lung damage and a more acute inflammatory response in presence of a pathogen, leading to aggravated

morbidity and mortality associated with lung infections: NO_2 [5,22-26], $PM_{2.5}$ [5,22,28,41-44], O_3 [40,45-47] and SO_2 [22] have all been shown to affect the lungs via one or more of the aforementioned mechanisms. No significant evidence can be found for carbon monoxide as a mediator for viral infection.

The primary limitation of this study does not control for individual exposure levels, as exposure is based on an average of pollutant levels across multiple measuring stations. The other limitation is the comparison between the influenza virus and SARS-CoV-2. While the viruses share many similarities, it is unknown how they react to air pollutants in ambient air or inside individual cells. We also acknowledge that the many statistical models created in this study may or may not be adequate, as there could be errors in disease classifications and environmental factors. The databases used to retrieve the aforementioned data, NACRS and NAPS respectively, both utilize systems to limit any disease misclassifications (NACRS 2020, [8]) or inaccurate pollutant data (NAPS 2020, [9]). There is also a risk of false positive or negative associations given the large number of hypothesis tests performed, however this is mitigated by applying a more stringent p-value.

CONCLUSION

Ambient air pollution exposure is associated with ED visits in this study. Specifically, exposure 3 days before ED visits was shown to have the largest number of the positive associations with ED visits for influenza and viral pneumonia. The presence of ground level ozone in the ambient air shows the largest number of the positive associations, where sulphur dioxide shows the second largest number of such associations. In a conclusion, urban ambient air pollution may be related to an increased number of ED visits for certain infectious diseases. This finding may be relevant to consider in the context of the ongoing SARS-CoV-2 pandemic.

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