

Original article

Is outdoor air pollution associated with physician visits for allergic rhinitis among the elderly in Toronto, Canada?

Background: While a number of studies suggest that air pollution is associated with allergic rhinitis in children, findings among adults have been equivocal. The aim of this study was to examine the relationship between outdoor air pollution and physician visits for allergic rhinitis among individuals ≥ 65 years of age in Toronto, Canada.

Methods: Physician visits were identified by using data from the Ontario provincial health insurance plan that is made available to all residents. Our analyses are based on 52 691 physician visits for allergic rhinitis among individuals ≥ 65 years of age in the Toronto metropolitan area between 1995 and 2000. Generalized linear models were used to regress daily counts of physician visits against daily measures of gaseous and particulate components of air pollution after controlling for seasonality, potential confounders (temperature, relative humidity, aeroallergens), overdispersion and serial correlation.

Results: A large number of comparisons were undertaken, with most showing no statistically significant associations between daily levels of air pollution and the number of physician visits for rhinitis. In contrast, an interquartile increase in the 10-day average of ragweed particles increased the mean number of daily rhinitis consultations by 6.4% (95% CI = 0.7–12.4%).

Conclusions: Our findings suggest that outdoor air pollution is a poor predictor of physician visits for allergic rhinitis among the elderly.

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Allergic rhinitis is a relatively common condition, the prevalence of which has been increasing in most industrialized nations (1, 2). It has been estimated that approximately 20% of European (2, 3), and 14% of American adults have allergic rhinitis (4, 5). This disorder carries with it a significant public health burden as measured by a lower quality of life (6, 7), detrimental effects on workplace (8) and school performance (9), medication usage (10), and increased comorbidity for other health conditions including asthma, hypertension, sinusitis and otitis media (11). While rhinitis does carry an important health care burden, it is also important to note that the associated lower quality of life can usually be improved through treatment (12).

Pollutants from vehicular traffic such as ozone, nitrogen dioxide and particulate matter have been linked to allergic responses. These particulate and gaseous components of air pollution can initiate and exacerbate cellular inflammation in both the upper and lower airways (13). For example, ozone has been shown to induce inflammation in the nasal airway, particularly in atopic individuals (14), and diesel exhaust particles have been shown to enhance an individual's response to allergens (15, 16). Nitrogen dioxide has also been shown to

promote an allergenic response in asthmatics (17–19). Air pollution may contribute to rhinitis by modifying the nasal mechanisms that allow the clearance of allergens from the nasal cavity (14).

There have been relatively few studies that have examined the association between outdoor air pollution and rhinitis. The authors of an ecological study in Leipzig and Munich, Germany suggested that differences in the prevalence of allergic rhinitis in children may be due to higher levels of nitrogen dioxide from car exhaust (20). Traffic-related air pollutants were found to be positively associated with self-reported and physician-diagnosed prevalence of allergic rhinitis among schoolchildren in Taiwan (21, 22). In contrast, a study of 2445 children in France found no association between the prevalence of rhinitis and regional levels of air pollution (23). Fewer studies have been conducted in adults. A study of 673 mothers in Virginia, USA examined exposures to a variety of outdoor air pollutants and found that only coarse particulate matter was related to an increased frequency of runny or stuffy nose (24). More recently, ozone and SO₂ were found to be important predictors of consultations with a general practitioner for allergic rhinitis (25); the observed associations were more

pronounced among children than adults, while a small number of daily consultations precluded an evaluation of the relationship in the elderly. As the elderly have been identified as potentially susceptible to the effects of air pollution (26), an examination of rhinitis outcomes in that age group could prove valuable.

While numerous health studies of air pollution have examined health outcomes using vital registry or hospital data, such an approach would be ill-advised for allergic rhinitis. Only in extremely rare instances would rhinitis be severe enough to warrant hospitalization, or cause death. As succinctly described by Hajat et al. (25), few studies have examined air pollution effects in a primary care setting. In addition, not only are the findings from previous studies equivocal, but they have also been limited by their use of self-reported data, deficiencies in assessment of air pollution exposure levels and sample size. To address some of the gaps in this research area, we report herein the results from a time-series study of air pollution and physician visits among adults, ≥ 65 years of age, in Toronto, Canada.

Methods and materials

Physician visit data

Daily counts of physician visits for allergic rhinitis between 1995 and 2000 were tabulated from the Ontario Hospital Insurance Plan (OHIP) database. This database contains patient-level claims information for all universally insured physician services that are provided free of charge to all eligible residents by the Ontario government. As part of an ongoing study, we were provided data for individuals ≥ 65 years of age. These data represent all insured services for which physicians are paid. Approximately 10% of physicians are on alternative payments for which there is little data available. The medical condition that is the principal reason for the medical visit is indicated on the claim by a three-digit ministry diagnostic code based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) coding system. The identification of allergic rhinitis visits was made using the ICD-9-CM rubric 177. Analyses were restricted to physician visits that occurred in the metropolitan Toronto area as determined using municipal residential codes recorded in the OHIP database.

Two important caveats warrant mention. First, only one visit per individual per day was included in the tabulation of the daily visit counts. Secondly, to exclude the possibility that the initial visit for rhinitis contributed to subsequent follow-up visits, we excluded visits that occurred within the 30 days subsequent to the initial consultation. Unfortunately, we were unable to distinguish between acute and regularly scheduled or follow-up visits.

Air pollution and weather data

Daily measures of air pollution for the Toronto area were calculated from fixed-site monitoring stations between 1 January 1995 and 31 December 2000. We examined associations between physician visits for both gaseous and particulate air pollution. Gaseous air pollutants examined included sulphur dioxide (SO_2), nitrogen dioxide (NO_2), ozone (O_3), and carbon monoxide (CO). Particulate matter is generally described based on size as determined by the

aerodynamic diameter. Coarse particulate matter ($\text{PM}_{2.5-10}$) consists of particles, the aerodynamic diameter of which ranges from 2.5 to 10 μm . Inhalable particles (PM_{10}) are those with an aerodynamic diameter of $< 10 \mu\text{m}$, while fine particulate matter ($\text{PM}_{2.5}$) are those with an aerodynamic diameter of $< 2.5 \mu\text{m}$. Particulate matter was measured using both the tapered oscillating micro-balance (TEOM) and dichotomous (DICHOT) sampling methods. A description of the differences, strengths and limitations of these methods are summarized elsewhere (27). TEOM data for PM_{10} and $\text{PM}_{2.5}$ were available for each day between 1 January 1998 and 31 December 2000. In contrast, DICHOT measures were available for $\text{PM}_{2.5}$, $\text{PM}_{2.5-10}$, and PM_{10} , on average, every sixth day over the entire study interval. O_3 and NO_2 samples were obtained from nine monitoring sites, seven of which provided measures of CO , and six measures of SO_2 . Dichotomous sampling of particulate matter occurred in four sites, while TEOM data for PM_{10} , and $\text{PM}_{2.5}$ were available in 10 and four sites, respectively.

Daily mean values were calculated by equally weighting data taken from all monitoring sites. With the exception of ozone, the daily mean values for the pollutants were used to examine associations between pollution and the number of physician visits. For ozone, the daily 8-h maximum value was used. The use of the daily 8-h maximum better reflects daytime highs as ozone is considerably lower at night; the use of a 24-h average would minimize differences between days with different daytime ozone concentrations. Daily mean temperature values for Toronto were obtained from Environment Canada. For relative humidity, the daily mean was calculated using hourly measures obtained at 6 AM and 3 PM.

Aeroallergen data

Aeroallergen data (pollen grains and fungal spores) for the Toronto area were collected using rotational impaction sampling methods. Particles that adhered to the silicon grease-coated sample rods were analysed to determine the number of particles present per cubic metre of air sampled. While data were collected for a variety of pollens and spores, we created a composite index that represents the sum of all counts from ferns, grasses, weeds and other unidentified pollens. These allergen data have been correlated with clinical outcomes including childhood asthma (28), and conjunctivitis and rhinitis (29). [For a more detailed description of the methodology used to collect aeroallergen data, refer to Dales et al. (28).]

Statistical methods

Time-series analysis based on generalized linear models was used to examine associations between the number of physician visits and fixed-site measures of air pollution. We first smoothed the time series to remove long-term seasonal patterns in the daily number of admissions, while retaining short-term patterns as they could be related to fluctuations in air pollution levels. Smoothing was done by using natural splines, as studies by Dominici et al. indicated that the use of locally weighted regression smoothing can produce biased estimates (30). This smoothing was performed while adjusting the model for day of week, and holiday effects through the use of indicator variables. We selected the temporal filter with a smoothing bandwidth (degrees of freedom) that produced a filtered time series that was consistent with a white-noise process as measured by Bartlett's test (31). The selection of the temporal filter in this manner minimizes the serial autocorrelation in the residual time series. The smoothing bandwidth requires a specification of the degrees of freedom which is equal to the number of knots + 2. For example, our final models were based on 218 degrees of freedom

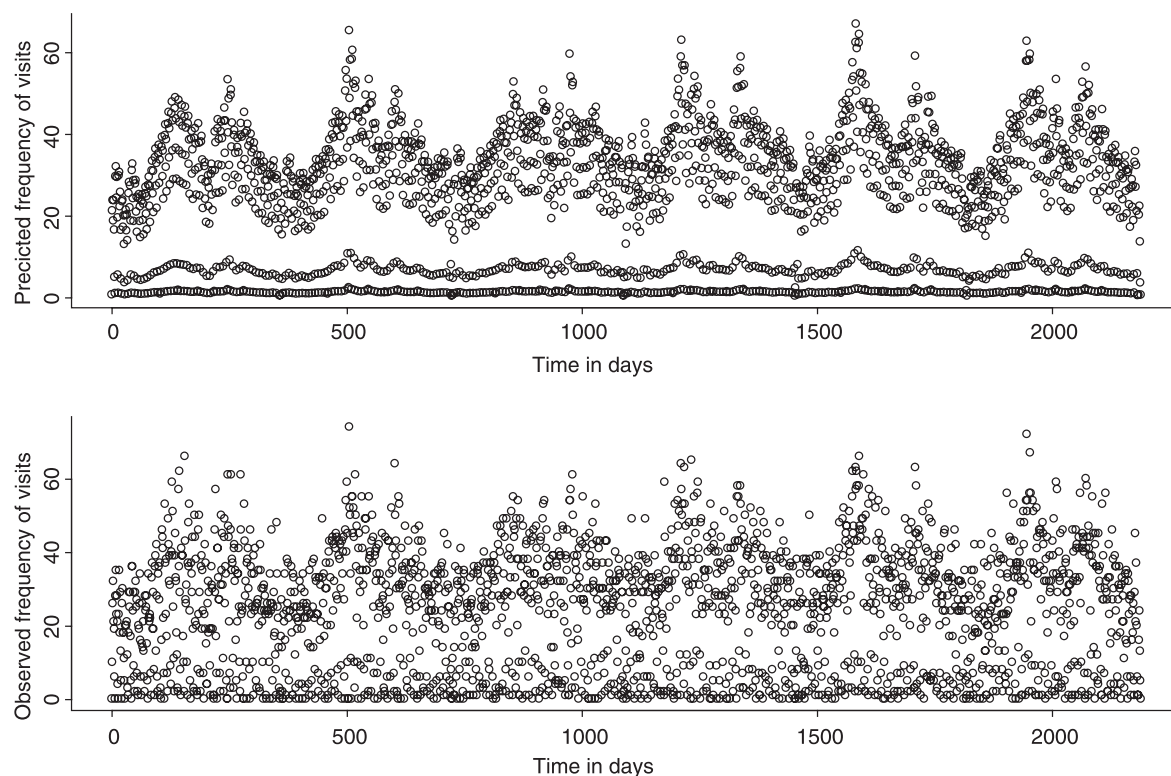


Figure 1. The observed and predicted number of daily (adjusted for temperature, relative humidity, daily number of physician visits for influenza, and allergen levels; particulate levels are based on TEOM measures) number of physician visits for rhinitis among patients ≥ 65 years of age, 1 January 1995 to 31 December 2000, Toronto, Ontario.

which assumed that there were 36 cycles in a year for 6 years ($218 = 6 \times 36 + 2$). The fit of each model was evaluated through an inspection of the partial autocorrelation function, the dispersion parameter, and plots of the residuals, observed and predicted values.

After smoothing, the per cent change in the number of physician visits was estimated for each pollutant, with adjustment for the daily mean temperature and relative humidity on the day of and preceding the visit using natural cubic splines with 2 degrees of freedom. The association between outdoor air pollution and rhinitis was also adjusted for daily levels of aeroallergens. The same models were applied to investigate the association between the frequency of physician visits and exposure to ragweed. These aeroallergens are widely recognized to induce allergic rhinitis in some individuals (32–34).

The per cent change in the number of physician visits that corresponded to an increase in the interquartile range (IQR; between the 25th and 75th percentile) was estimated for each pollutant. The IQR was calculated based on the frequency distribution of the daily pollution levels observed during the study period. Time-series studies of air pollution frequently use the IQR in such a fashion that it facilitates comparisons between individual pollutants that are measured on different scales. We also examined associations between physician visits and lagged exposures to air pollution. Specifically, we examined the relationship between the number of physician visits and air pollution levels on the same day, as well as for levels observed for each of the 6 days that preceded the visit. The associated lower and upper 95% confidence intervals of this percentage change were obtained by assuming that the estimated regression coefficients were normally distributed, while correcting the estimated standard errors for

non-Poisson dispersion. Consistent with numerous other air pollution studies, stratified analyses were also undertaken by season, as it is well recognized that activity patterns change, along with air pollution levels, by season. This was undertaken by splitting the calendar year into two equal 6-month periods (May to October, and November to April). Given that ragweed exposures were only observed between July and October, analyses correlating this exposure to physician visits were restricted to these months. All statistical analyses were conducted using S-PLUS software (35).

Results

As expected, the data indicated strong seasonal and day of week variations in the number of physician visits for rhinitis with peaks occurring during the summer months (Fig. 1). Our analyses are based on a total of 52 691 visits occurring between 1 January 1995 and 31 December 2000. Only 5% of these visits occurred on weekends (Saturday or Sunday).

Daily air pollution levels observed in Toronto over the study period are summarized in Table 1. Dichotomous measures of air pollution were available for only approximately 20% (452/2190) of the study days. While dichotomous sampling was performed for the most part on every sixth day, additional measures were obtained during the non-winter months. In particular, dichotomous

Table 1. Mean, standard deviation and range of air pollutants and daily numbers of physician visits for respiratory disease, between 1 January 1995 and 31 December 2000, Toronto, Canada

Variable (unit)	Days	Mean	Standard deviation	Min.	Max.	IQR
Air pollutant						
NO ₂ (ppb)	2190	25.4	7.7	9.2	71.7	10.3
O ₃ -8 h max. (ppb)	2190	30.0	15.4	1.8	98.7	19.4
CO (ppm)	2190	1.1	0.4	0.0	2.2	0.4
SO ₂ (ppb)	2190	4.7	2.8	0.0	24.8	3.2
PM ₁₀ (DICHOT) (g/m ³)	452	23.6	10.9	3.1	71.7	14.1
PM _{2.5} (DICHOT) (g/m ³)	452	12.8	7.6	2.5	54.8	9.5
PM _{2.5} -<10(DICHOT) (g/m ³)	452	10.8	5.6	0.5	32.8	7.1
PM ₁₀ (TEOM) (g/m ³)	1095	16.4	4.9	7.6	50.8	5.7
PM _{2.5} (TEOM) (g/m ³)	1095	7.7	3.3	2.4	25.2	3.8
Weather						
Mean temperature (°C)	2190	8.4	10.5	-19.8	30.4	17.1
Relative humidity (%)	2190	70.2	12.1	31.5	99.5	16.5

IQR, interquartile range.

ous sampling measures were available for a total of 274 and 178 days, for the periods of May to October, and November to April, respectively.

Figure 2 summarizes associations between physician visits for rhinitis observed over the course of the entire year and gaseous and TEOM-based measures of particulate matter. No statistically significant associations were observed between daily visits for rhinitis and pollution

levels as measured on the day of the visit, nor for any of the 6 days preceding the visit.

Similarly, no statistically significant associations were observed for visits occurring between May and October (Fig. 3), nor for those occurring between November and April (Fig. 4). The results of our analyses comparing dichotomous measures of particulate matter to the frequency of physician visits are displayed in Fig. 5. The small number of dichotomous sampling measures available for the period between November and April did not allow for these risks to be estimated.

Because no association was found between air pollution and physician visits, we evaluated whether our time-series model could detect associations for ragweed. Ragweed (*Ambrosia*) is recognized as one of the most common triggers of allergic rhinitis (36). We restricted analyses to those parts of the year (between 1 July and 31 October) when positive counts of ragweed were observed; the results from these analyses are presented in Table 2. Ragweed particulate levels were positively associated with the frequency of physician visits, and this risk was most pronounced for extended periods of high ragweed levels. Specifically, the mean percentage increase in the number of daily physician visits for rhinitis associated with an interquartile increase in ragweed particles was higher based on the 10-day mean, rather than metrics constructed using shorter time intervals.

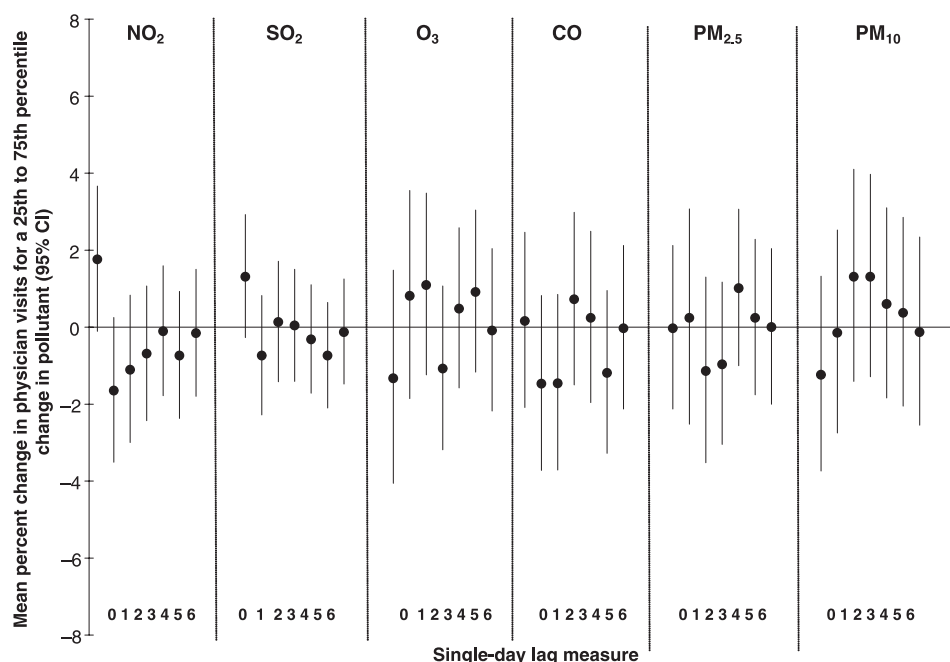


Figure 2. Percentage change (and 95% confidence interval; adjusted for temperature, relative humidity, daily number of physician visits for influenza, and allergen levels; particulate levels are based on TEOM measures) in the number of consultations with physicians for rhinitis, among adults ≥ 65 years of age, associated with a 25th to 75th percentile increase in air pollution for single-day measures on the day of consultation and 1–6 days prior to consultation, metropolitan Toronto area, 1995–2000.

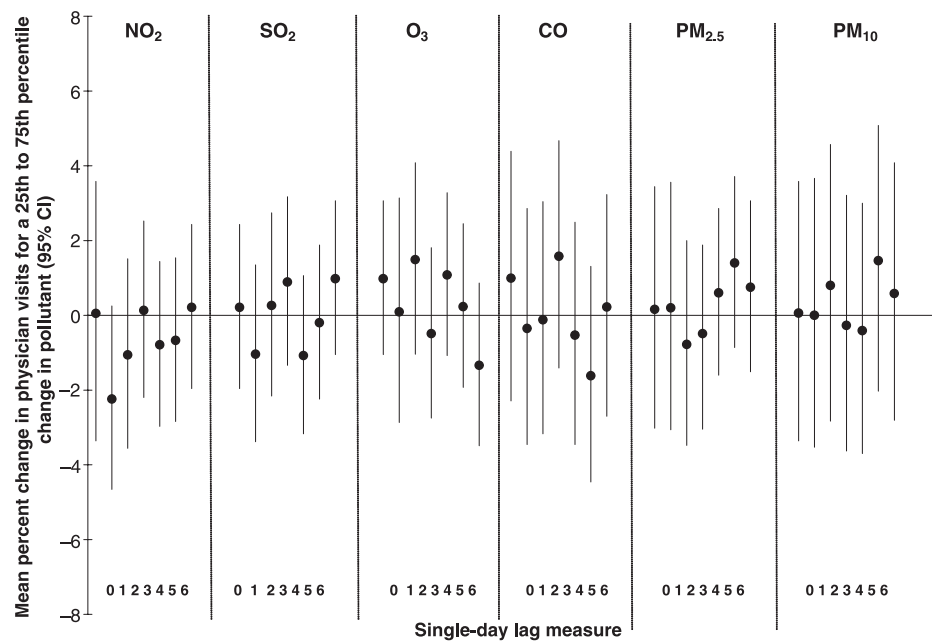


Figure 3. Percentage change (and 95% confidence interval; adjusted for temperature, relative humidity, daily number of physician visits for influenza, and allergen levels; particulate levels are based on TEOM measures) in the number of consultations with physicians for rhinitis, among adults ≥ 65 years of age, associated with a 25th to 75th percentile increase in air pollution for single-day measures on the day of consultation and 1–6 days prior to consultation, metropolitan Toronto area, between May and October, 1995 to 2000.

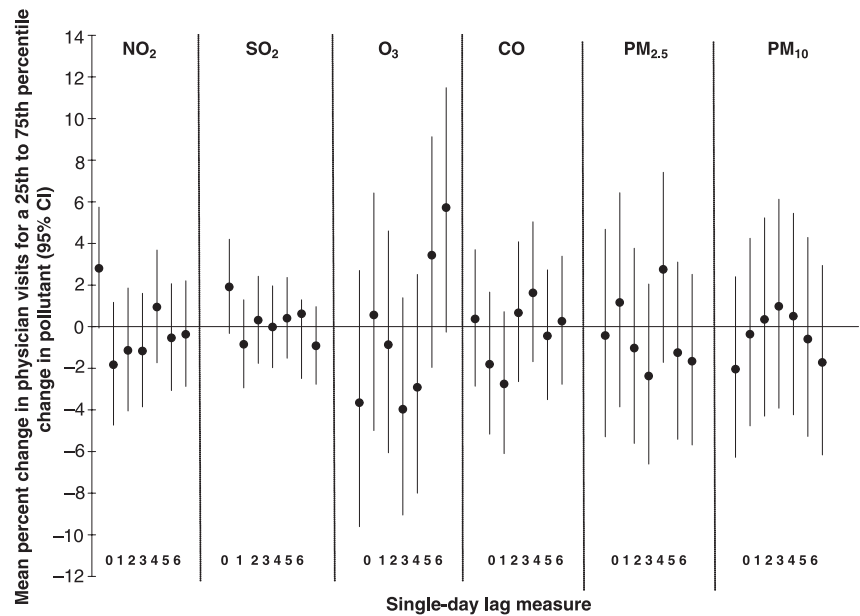


Figure 4. Percentage change (and 95% confidence interval; adjusted for temperature, relative humidity, daily number of physician visits for influenza, and allergen levels; particulate levels are based on TEOM measures) in the number of consultations with physicians for rhinitis, among adults ≥ 65 years of age, associated with a 25th to 75th percentile increase in gaseous pollutants for single-day measures on the day of consultation and 1–6 days prior to consultation, metropolitan Toronto area, between November and April 1995 to 2000.

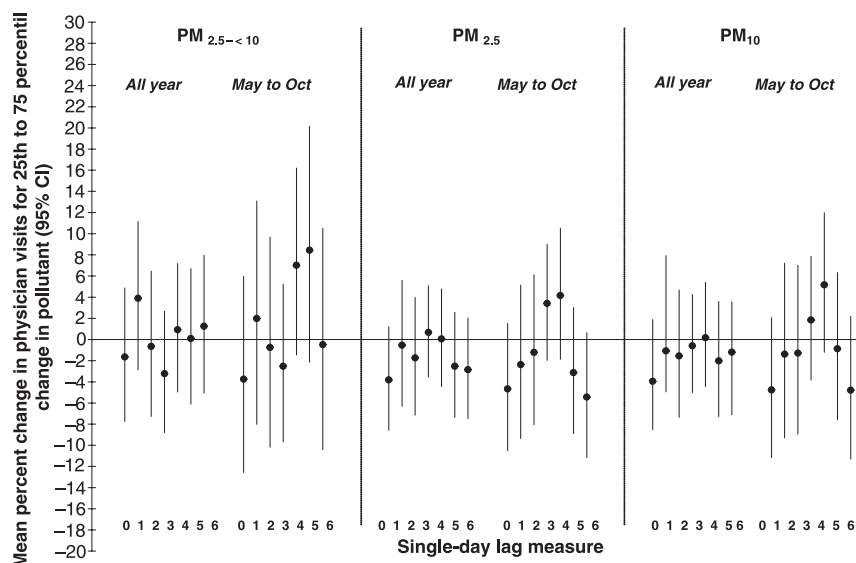


Figure 5. Percentage change (and 95% confidence interval; adjusted for temperature, relative humidity, daily number of physician visits for influenza, and allergen levels) in the number of consultations with physicians for rhinitis, among adults ≥ 65 years of age, associated with a 25th to 75th percentile increase in particulate matter based on dichotomous sampling for single-day measures on the day of consultation and 1–6 days prior to consultation, metropolitan Toronto area, for the entire year and between May and October 1995 to 2000.

Table 2. Percentage change (and 95% confidence interval) in the number of consultations with physicians for rhinitis, among adults ≥ 65 years of age, associated with a 25th to 75th percentile increase in ragweed* based on a 1, 3, 5, 7 and 10 day average between 1 July and 31 October 1995 to 2000

Ragweed exposure metric in relation to:	Mean percentage change	
	%	95% CI
Daily mean on day of visit	0.1	–1.0 to 1.2
3-day average	0.5	–1.2 to 2.2
5-day average	0.7	–1.2 to 3.3
7-day average	2.5	–0.4 to 5.7
10-day average	6.4	0.7 to 12.4

*The mean percentage change based on a increase of 22.6 particles per cubic metres corresponds to the interquartile daily range during ragweed season; adjusted for temperature, humidity and influenza visits.

Discussion

This study makes use of a population-based administrative database to examine the relationship between air pollution and ragweed levels and physician visits for allergic rhinitis. The coverage of the database is believed to be excellent given the universal health care insurance that exists in the province of Ontario, and because reimbursement of physician claims are handled through the OHIP programme. As a result, the design of the study ensures that our risk estimates are not unduly influenced by selection bias. Moreover, this database does not rely on subjective self-reported symptoms reported by participants. Rather, our outcomes are based on counts of daily

physician visits where the diagnosis was made by a trained health professional. This is an important strength relative to other studies. It is however important to note that approximately 25% of the claims in the OHIP database (excluding laboratory services and diagnostic testing) do not have a specified diagnostic code. However, we know of no reason as to why the frequency of physician visits with missing diagnostic coding would be associated with air pollution level, a condition necessary to bias our results.

In this study, a large number of comparisons were undertaken and, for the most part, no clear pattern of association between outdoor air pollution levels and physician visits for rhinitis was evident. While a few statistically significant findings were noted, these must be interpreted cautiously. Air pollution studies will frequently be plagued by issues of multiple comparisons as associations between exposure and health outcomes are invariably examined for a large number of pollutants, often using several different cumulative and lagged exposure metrics. As a result, there is an increased probability of detecting a statistically significant finding by chance alone; consequently, there is a greater opportunity for spurious results to be reported. While one approach to multiple testing advocates using more stringent *P*-values to account for a larger number of comparisons being undertaken, this approach has been described as causing more problems than it intended to solve (37), and was not used here.

For several reasons, our analyses strongly support an association between ragweed exposure and physician

visits for rhinitis. The strength of the association was stronger than for air pollutant measures, it was consistently observed for a number of exposure metrics, the magnitude of risk was directly correlated with cumulative exposure, and statistical significance was achieved. As ragweed exposure is known to induce rhinitis in some individuals, this result suggests that our models are sensitive enough to detect a known trigger. Perhaps, more importantly, taken together, our analyses suggest that air pollution exerts at most a minor effect for the exacerbation of rhinitis in the general population as defined by those aged ≥ 65 years.

We made an attempt to extend our analyses to examine the combined effects of air pollution and exposure to ragweed on the frequency of physician visits for allergic rhinitis. No statistically significant first-order interaction was found for terms consisting of ragweed exposures and 1-, 3- and 5-day average levels of NO₂, SO₂, CO or particulate matter. These findings should be interpreted cautiously given that there was limited statistical power to evaluate effect modification as positive ragweed levels were only observed during 4 months of the year (July to September).

The time-series design of the study is well suited to evaluate associations between short-term variations in pollution and health outcomes in a given geographical area. An important strength of this design is that the population serves as its own control, as confounding by population characteristics (e.g. smoking, sociodemographic characteristics) is negligible as they are quite stable from day to day (38). In this context, an elderly patient's allergy history can be regarded as stable, and here, the time-series method can determine whether allergen exposure can produce acute effects among those who resided in the Toronto area between 1995 and 2000. Had we been able to identify individuals whose medical histories indicated an allergic response to ragweed, our risk estimates for ragweed exposures in this subgroup would like have been higher.

The absence of an air pollution association may be partly due to our inability to capture those physician visits that were acute *vs* those that were regularly scheduled examinations or follow-up visits. If air pollution does indeed exacerbate rhinitis, delays in the scheduling of a physician visit, could obscure a temporal association between daily levels of air pollution and the frequency of physician visits. Under such a scenario, the ability to characterize the association for a region such as Toronto is made even more difficult as scheduling delays are likely to differ considerably across practices, and possibly according to the physician-perceived health status of a particular individual. The ability to detect an association between outdoor air pollution levels and rhinitis may also be hindered by the tendency of individuals who have rhinitis-related symptoms to manage symptoms on their own rather than seek consultation with their physician. Over-the-counter medications are

frequently used to treat symptoms of allergic rhinitis. Previous studies also suggest that individuals frequently manage their allergic rhinitis. For example, in France, Didier et al. found that nearly one of five patients with typical rhinitis symptoms had never visited their physicians specifically for their nasal problems (39). Similarly, in the UK, only 18% of subjects with rhinitis had visited their physician concerning their hay fever during the past 2 years (40). In the context of the above arguments, our finding of an association between ragweed exposure and physician visits for rhinitis is particularly compelling. In particular, the above arguments suggest that the true association between ragweed exposure and the occurrence of allergic rhinitis is greater than reported.

Like most other time-series and case-crossover studies, our risk estimates may be biased through the use of regional (ecological) ambient measures of air pollution to infer individual exposure. Although such measures may be crude, ambient levels are often the only feasible method of obtaining measures with respect to cost and burden to the study participant (41). However, this approach assumes that each individual in the region has the same exposure, and is unable to capture differences in activity patterns, or variations in pollution levels within urban areas. Swartz et al. argued that because the health outcomes are tabulated over the population in a time-series design, the relevant exposure measure is the mean of personal exposures on that day; this mean is probably more highly correlated with central monitoring exposures than individual exposures (42). Moreover, the probable consequence of using ambient concentrations is an underestimation of air pollution effects (43). It follows that, for a real association, risk estimates calculated in this manner may be understated.

The design of our study was similar to that undertaken by Hajat et al. (25). They found associations between daily consultations for rhinitis among adults and NO₂, SO₂, ozone, PM₁₀ and black smoke. While their study adjusted for the effect of some aeroallergens, they did not explicitly look at the relationship between ragweed and rhinitis consultations. We observed positive associations between allergic rhinitis and SO₂ and NO₂ for exposures occurring on the same day as the physician visits, and only during the winter time. Differences in the composition of the pollution between cities may have partly contributed to differences between our risk estimates. Other important differences between their study and our own include our exclusion of visits occurring within 30 days of the initial consultation, our restriction to physician visits among those ≥ 65 years of age, and cultural differences in health care utilization practices.

The findings of Hajat et al. (25), as well as other studies (21, 22, 44) suggest that outdoor air pollution can affect the presentation of rhinitis in children to a greater extent than in adults. Relative to individuals ≥ 65 years of age, children are more likely to spend a greater proportion of their time outdoors undergoing some form of physical

activity. Furthermore, they have smaller airways, and less developed respiratory symptoms that could leave them more vulnerable to air pollution. Moreover, when compared with adults, they may be more likely to be brought to a physician as result of exhibiting rhinitis-related symptoms than adults experiencing the same symptoms. Unfortunately, we only had physician visit data for those ≥ 65 years of age, and were unable to perform analyses among children. We recommend that this work be pursued.

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