Statistical modeling of complex health outcomes and air pollution data: Application of air quality health indexing for asthma risk assessment

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DOI: ***10.2427/12092***
Accepted on January 27, 2017

ABSTRACT

Background: When fitting statistical models for complex health outcome data; zero inflation, autocorrelation, confounding, and seasonality play an important role in accurately assessing air pollution risk, especially when using such model estimates for national air quality health indices (NAQHI) formation. NAQHI generalizes model estimates across all geographies and seasons and neglects area and season specific variations. The aim here is to develop complex statistical models, specific to the data structures and to demonstrate effectiveness of these model estimates in public health message delivery using NAQHI.
Methods: I fitted zero inflated, auto regressive, Poisson and Negative Binomial models with lagged effects for sparse asthma admissions and ambient air pollution data and compared the model risk estimates with that of the NAQHI. Data came from two sites, Halifax, an urban, traffic and industry polluted site and Sydney, a rural waste disposal polluted site, in the province of Nova Scotia, Canada. Data complexity structure was assessed by comparing the estimates with and without each structure.
Results: NAQHI used three pollutants, Nitrogen Dioxide, Ozone and particulate matter. I found Carbon monoxide in the urban site and lead in the waste disposal site as prominent pollutants with significant seasonal differences. The findings demonstrated severe under-assessment of asthma admission relative risk by NAQHI, when auto correlation and zero inflation are ignored whereby prominent pollutant effects are omitted.
Conclusion: This study demonstrated the importance of complex statistical model use and the consequences of not consideration of specific data structures in public health risk assessments.

Key words: negative binomial model, Poisson model, confounding, time series data, air quality health index

INTRODUCTION

Epidemiologic assessments of the association between ambient air pollution exposure and asthma morbidity have produced inconsistent results in different areas with diverse pollutant sources. Additionally, the discrepancies between site specific research findings may be due to divergence of data structures arising from seasonal

variations, zero inflation, autocorrelation and confounding among pollutants and between meteorological conditions and not using the appropriate statistical models that incorporate this complex data structures. The situation threatens national air quality index (NAQHI) development and use. This paper introduces statistical models that incorporate aforementioned complex data structures that are common in time series of sparse health outcomes and demonstrate the importance of use of such models in public health risk assessment. Though NAQHI, a health risk assessment index, is applicable to a wide spectrum of diseases that can be impacted by pollution exposures, the present investigation is only on asthma. The statistical methods described herein can be applied to any health outcomes and exposures with similar data structures.

This paper will contribute to the epidemiologic knowledge on air pollution health risk assessment in areas with sparse asthma hospital admission data, emphasizing the need for site-season specific pollution index development that account for zero-inflated, ARIMA models. The present study asthma risk assessment is based on the human health hazardous gaseous and particulate pollutants in the environment, using ambient levels (that exceed thresholds) of sulfur dioxide (SO_2), carbon monoxide (CO), nitrogen dioxide (NO_2), ozone (O_3) and particulate; total suspended particulates (TSP), particulate matters (PM_{10}) and lead (Pb) levels. Those pollutants have been identified by the United States Clean Air Act as endangered to public health, if exceeded specific threshold levels specified by the act [1]. Therefore, national air quality standards have been established for those pollutants [2]. Though ambient pollutant levels do not provide accurate personal exposures, they have been used as surrogate measures for public health risk assessment and warning message delivery, due to ease of availability. In Canada, routine random testing is done for a multitude of pollutants and the ones that exceed minimal acceptable standards (thresholds) will be continuously monitored. This continuously monitored pollutant level data are available for public use. Therefore, all pollutants included in the present analyses have recorded levels higher than the Canadian national acceptable standards [3] at some point during the random testing.

Air quality health indices are primarily used as predictors of environmental health risk. The Canadian NAQHI is based on a mathematical formula that combines, O_3, particulate matters (less than 2.5 $\mu g/m^3$ PM2.5 or less than 10 $\mu g/m^3$ PM_{10}) and NO_2 into one index with scaled values ranging from 1-10 [4]. The index is extensively used for Canada wide public health warning message delivery. The combination of pollutants in NAQHI varies by country. The Chinese index uses PM_{10} and NO2 [5]; the Russian index includes formaldehyde, CO and TSP [6] and PM_{10}; SO_2 and NO_2 are used in the European regional index [7]. I was unable to find research based evidence on intra country spatial variations of the index. When building those national indices, seasonal variations were ignored even in countries, where there are strong seasonal weather patterns. Zero inflation that arises in "small" area level health outcomes is unique to less populated areas and this feature was not taken into consideration in the national index development efforts. The two sites of interest of this paper were excluded from the Canadian NAQHI development process due to unavailability of $PM_{10/2.5}$ data at the time of the index development [8]. But the Canadian government websites use the index to calculate and deliver public health risk assessments and warning messages throughout the country [9]. The NAQHI was originally developed based on mortality data and the researchers who developed the index carried out sensitivity analysis and found that the index is sensitive to asthma morbidity risk assessment [8]. Later other researchers have shown that the index derived risk estimates were significantly predicting asthma morbidity, emergency visit, hospital admission and outpatient visit risks, in densely populated areas, where the mortality and pollution data were used for the index development [10, 11]. Szyszkowicz and Kousha (2014) found Canadian NAQHI as a significant predictor of asthma emergency visits in Windsor, Ontario, Canada [11]. Hospital admission for asthma is of particular interest of this paper. To et al. (10) analysed Ontario provincial data comprising more than one third of Canada population. They supported the use of Canadian NAQHI as a chronic disease mobility risk index showing NAQHI's ability to assess asthma hospital admission risk, indicating that the risk ratio significantly increased with each unit increment of Canadian NAQHI. Findings of those two studies came from large population based analysis and from the areas where the data were contributed to the index development. My research was motivated by the above two studies to investigate the relationship between NAQHI and asthma hospital admissions in two Canadian sites with small population densities and the data from the two sites were not used in the NAQHI development. This paper includes a statistical model building and epidemiologic assessment exercise with an analytical critique and/or appraisal to interrogate or support the wide overuse of air quality health indices geographically and making generalizability of the index use across different health outcomes.

The pollutants included in the present research were all shown to have significant effects on asthma in different areas but the compositions and combinations are site and season specific. Worldwide literature supports the effect of CO on asthma hospital admissions and a confounding effect with O_3 [12, 13] as well as its' seasonal significance in the warm seasons were also found [12-18]. O_3 formation is dependent upon warm weather and CO is a precursor for O_3. SO_2 and asthma morbidity significance is masked by its correlation with particulate matters and O_3 [12, 14, 17-19]. CO and asthma association is known to be masked by NO_2 [8]. Short-term PM exposure had indicated

increased risk of morbidity (hospitalizations and emergency visits) with (lag period 2-3 days) and also increased risk of mortality due to respiratory conditions [13, 17, 20-25]. Ambient Pb exposure and its association with asthma morbidity, among humans, were not extensively studied except in cases, where lead poisoning related asthma attacks among children in which significant effect was justified [26]. A review article showed that the mechanism that connects lead exposure to asthma was through oxidative stress and immune and inflammatory response alternations [27]. Given that there are clinical evidence, Pb exposure is included in the present statistical modeling exercise. Effect of seasonal weather changes on asthma and above mentioned pollutants were confirmed in other ecological studies [15, 28, 29]. Therefore confounding with climatic conditions were included in the statistical models in the present study.

Significance of the use of asthma hospital admissions, the two study sites and the selection of the study period, are worth explanations. Among several asthma health outcomes that have been studied hospital admissions have the unique advantage (over emergency room and general practitioner visits) to be a reliable health outcome measure given that the person voluntarily sought a physician's medical advice due to symptom exacerbations prior to being admitted to the hospital, at which point the diagnosis of asthma is justified [19]. Death may not be the immediate effect of air pollution, but an asthmatic is admitted to the hospital prior to death and hospital admission provides a better indicator to be used in early health risk assessments to deliver public health warnings.

The two sites are situated in the province of Nova Scotia (NS), Canada, with notably high rates of asthma hospital admissions [30]. During the study period, the Sydney area in NS had tar ponds (a waste disposal site of coke ovens and steel manufacturing plants) and the surrounding areas were known to be Canada's worst contaminated sites, even decades after closing down the pollutant generating industries [31]. In Sydney, the presence of lead, arsenic and polycyclic aromatic hydrocarbon were noted by researchers [31] but no studies have examined ambient air pollution and asthma hospital admissions. Whereas the Halifax site, situated in the capital city of the province of Nova Scotia (NS) was noted as having highest (among those living in six other Canadian cities) prevalence of wheezing among children and the researchers noted heavy exposure to traffic as the associated environmental health risk factor [32]. In addition to the noted traffic pollution in Halifax, there are harbour pollutions, pollution due to poor waste management, ship emissions, burning of oil for power generation, the refinery emissions and coastal smog conditions. Thus Halifax provides a prime site for urban pollution studies. The two sites bring perspectives on urban pollution (Halifax) and waste disposal pollution (Sydney).

The study period of 1990-1998 was selected due to three reasons; the completeness and accuracy (since the database was validated for this period) of the asthma admission data for both sites, there were no environmental catastrophes noted for the study sites during this period and finally this period overlaps the study period of Canadian AQHI index formulation, 1981-2000 [8]. Therefore, ecological relationships that occur in a natural exposure setting can be explored and a direct comparison with the NAQHI risk assessment is warranted within the study period.

The primary objective of the present study is to develop zero inflated Poisson/Negative Binomial ARIMA model based estimates for air quality health risk assessment indexing and to compare the results with NAQHI. Lastly I aim to carry out an analytical critique to interrogate the consequences of neglecting particular data related complexities; auto correlation, seasonality, confounding, zero inflation and exposure effect dispersed over distributed lag times in the formulation of air quality health indices.

METHODS

Data

Daily hospital admissions of residents admitted to hospitals for asthma, in the two study sites were extracted for the period 1990 to 1998, from the NS provincial Medical service insurance (MSI) database which capture complete and accurate hospital admissions in the province since all services are paid through MSI. The International classifications of disease, Ninth Revision (ICD-9) codes listed for asthma under 493.00 to 493.91 were used for the identification of asthma [33]. Hospital admission data were extracted using postal codes surrounding the air pollutant monitoring station and included approximate areas of 97.2 square kilometer in Halifax, the capital city, with only one tertiary care hospital and 25.2 square kilometer area in Sydney with a low population density. Researchers have used 100 [34] and a 144 square kilometer areas grid [2] surrounding the monitoring station as exposure area coverage. The atmospheric temperature, humidity/precipitation, wind speed, rain fall and snow data were obtained from the Atmospheric Environmental Service monitoring stations in each study area and were used as confounders. Pollutant data, in the two monitoring stations of each site were obtained from the Department of Environment, Canada and the Provincial Department of Environment and Labour. The monitoring stations collect hourly means of O_3, CO, NO_2, SO_2 and TSP in Halifax and Pb, TSP, PM_{10}, SO_4, SO_2 in Sydney. Given that cumulative exposures are needed for symptom exacerbation, a cumulative exposure for the entire day (24 hours) was used for the statistical modelling. A 6 day moving average smoother eliminated the missing value problem for this data that were collected once in 6 days.

Statistical analysis

Zero inflated Poisson/negative binomial autoregressive models (ZIP autoregressive or ZINB autoregressive model) were fitted to the asthma hospital admission daily totals and autoregressive terms and pollution distributed lags up to 2 days were added to the models. Akaike's Information Criteria (AIC) that gave a minimum value guided the best model [35]. In what follows, X_{kt} represents the daily cumulative exposure of the kth pollutant at day t. To take into account the variation of hospital admissions due to clinic closures on weekends, a weekday indicator variable was included in all of the models.

ZIP autoregression is a combination of methods used for zero inflated Poisson (ZIP) regression and autoregression models. Daily counts of hospital admissions data, often violates Poisson assumption of equality of the mean and the variance due to excess zero admission days, a concept known as zero inflation [36]. ZIP model was first introduced by Lambert (1992) to model defected manufacturing products [37] and later the model was extended to use in healthcare utilization data [38]. Lambert (1992) showed how the maximum likelihood method can be used to estimate ZIP regression model co-variate estimates using EM algorithm [37]. Using simulated data, the application of the zero inflated auto regressive time series model to assess hospital admission risk from air pollution were proven to provide optimum results [39, 40].

ZIP model is a two-component mixture model that can be described as follows. Let the asthma admission on the day t is Yt then Yt takes values from 0, 1, …., n.

Let $P(y_t|X_t)=P_t(0)$ then $P(y_t>0|X_t)=1-P_t(0)$ where Xt represents pollution variables vector at time t. The zero inflated part (ie. whether or not $Y_t=0$) is modelled using the logistic link function with a Binomial distribution and the non-zero part $P(y_t>0|X_t)=1-P_t(0)$ is assumed to follow Poisson distribution with log link [41]. For simplicity AR(1) presentation is given below.

If the conditional distribution of the ZIP process has the mean then

$$P(Y_t|X_t,Y_{t-1}) = (1-P_t(0))\frac{\exp(\mu_t)\mu_t^{y_t}}{y_t!} \text{ for } y_t>0 \text{ and}$$

$$P(Y_t|X_t,Y_{t-1}) = (P_t(0))\exp(-\mu_t), \text{ for, } y_t=0.$$

The zero inflated part is modelled using a logistic link function,

$$logit(p_t(0)) = \gamma Y_{t-1} + \sum_{k=1}\sum_{j=0}\beta_{kj}X_{k(t-j)} \quad (1)$$

and the non-zero model is given by

$$\log(\mu_t) = \alpha y_{t-1} + \sum_{k=1}\sum_{j=0}\gamma_{kj}X_{k(t-j)} \quad (2)$$

Without loss of generality it is assumed that for stationary models the autocorrelation at lag 1 is stable whether the correlation is between 0 counts followed (or preceded) by greater than 1 counts or otherwise. Therefore the coefficient representing AR(1) parameter estimates represent lag 1 autocorrelation, γ *in equation* (1) *and* α in equation (2), are equal for a stationary processes [39, 40]. I used Dickey and Fuller (1979) test to test the stationarity of the process [39].

Negative Binomial distribution is used when Poisson assumption of homoscedasticity (simply put when Mean=variance) is violated. Homoscedasticity was check by the departure of the ratio,

$k = \frac{Deviance}{degrees\ of\ freedom}$ from 1, in which case the negative binomial distribution was used. Where

$$P(Y_t|X,,Y_{t-j}) = (1-P_t(0))\frac{\Gamma(y_t+\frac{1}{k}))k^{yt}\mu_t^{yt}}{\Gamma(y_t+1)\Gamma(\frac{1}{k})(1+k\mu_t)^{y_{t+}(\frac{1}{k})}},$$

for $y_t > 0$, and k is the negative binomial dispersion parameter.

More general expression for an autoregressive process of order greater than 1 can be written as follows.

The general logistic model with lagged variables is given by

$$logit(p_t(0)) = v_t + \sum_{k=1}\sum_{j=0}\gamma_{kj}X_{k(t-j)}$$

Similarly, the Poisson autoregressive model fitted was

$$\log(\mu_t) = u_t + \sum_{k=1}\sum_{j=0}\beta_{kj}X_{k(t-j)},$$

where $X_{k(t-j)}$ indicates daily cumulative exposure at day t-j for the kth pollutant and j=0, 1,2,.., depending on the lag time. The notation of v_t and u_t represents a linear combination of lagged variables of Y_t depending on the order of AR process. The joint likelihood was maximized using Newton-Rapson method that uses a penalized likelihood approach. More details of the zero inflated time series count data modeling are given by Hasan et al (2012) [40].

Model selection

I included the weekday variable, meteorological factors, in the zero inflated Poisson/negative binomial auto regressive and logistic models as confounders. Minimum AIC was used to select the best model using one by one backward elimination of variables with the highest p-value. Relative risk was interpreted for the increment equivalent to inter quartile range (IQR) increase that has been done elsewhere [28, 29, 42].

Data analysis and Computational support

The data were analysed using SAS software version 9.3 [39].Eight models were fitted for each of four seasons

and for the two sites. The time-series plots showed only the observed data with random missing imputed values. I used the methods described in Hasan et al. (2012) to fit Zip models to the time series of emergency room visits and air pollution data. To make computations simple, I followed a two-step process of first identification of the time series model with estimates for the hospital admission time series and then fitting a ZIP model using SAS proc countreg procedure [43].

RESULTS AND DISCUSSION

There were 0-11 admissions (per day) in Halifax, with a daily average of 2.15 (SE=0.032). Daily mean for the Sydney site was 1.02 with se=0.02, 38% zero admission days with 0-7 admissions per day. Figure 1 contains mean hospital admissions for each season of the year with vertical bars showing corresponding confidence intervals. That shows a seasonal pattern with the lowest values in the summer and the highest values in the fall of each year. In Halifax, there were 36% zero admission days in the winter and spring seasons and 46% days in the summer. The downward annual trend that is apparent (figure 1) was also shown in other Canadian studies and the researchers noted this as resulting from increased asthma management efforts and hospital bed reductions [44]. I argue that if that is the case with these sites this should occur in all seasons of the year. Confidence intervals (CI) shown in figure 1 overlapped across years and seasons and therefore downward trend cannot be statistically justified. Here the patterns may be due to other reasons such as pollution control mechanisms since the statistical significance of the trend appeared only in the winter time ($p<0.0001$). Therefore, the seasonal models were fitted without trend removal.

Multi pollutant ZIP, autoregressive, distributed lag models by season: Eight models, four for each of the study site corresponding to each of the four seasons were fitted.

Four seasonal models fitted for Halifax are listed under equations (3)-(6) below and for Sydney are listed under (7)-(10). Of all the meteorological variables included in the models, there were considerable amount of confounding and only the temperature showed a significant effect and that was also only shown in the zero inflated part of the model. Figure 2, 3 shows the relative risk (RR) of hospital admissions for an unit increment for Halifax and Sydney pollutant levels for the non-zero model. The zero model did not show any significant pollutant effects. Numerical results for Halifax and Sydney for IQR increments are shown in Table 1. Note that, in Table 1, the multipollutant models with 24 hour cumulative exposure for certain variables are noted as redundant due to lack of variation over the study period when adjusted for other variables.

The four final models with estimates (nearest 4th decimal place) for the Halifax urban site are presented as follows (Table 1 depicts RR, for IQR increment, and CI for each model equation listed in 3-10). Note that the confounder temperature was excluded in the model presentation below.

$$\text{Winter: } log(\mu_t) = 0.033y_{t-1} + 0.0151(CO)_{t-2} + 0.0007\,(NO2)_t - 0.0008\,(SO2)_t + 0.0011(TSP)_{t-1} + 0.0002(O3)_t \quad \text{.....(3)}$$

$$Spring: log(\mu_t) = 0.056y_{t-1} + 0.0373(CO)_t + 0.0009\,(NO2)_t + 0.0001\,(SO2)_t + 0.0005(TSP)_{t-1} - 0.0004(O3) \quad \text{.....(4)}$$

$$\text{Summer: } log(\mu_t) = 0.155y_{t-1} + 0.0098(CO)_{t-1} + 0.0014\,(NO2)_{t-2} - 0.0014\,(SO2)_{t-2} + 0.0011(TSP)_t - 0.0002(O3)_{t-2} \quad \text{.....(5)}$$

$$\text{Fall: } log(\mu_t) = 0.047y_{t-1} + 0.0099(CO)_t - 0.00710.0099(CO)_{t-1} + 0.0092(CO)_{t-2} + 0.0011\,(NO2)_{t-2} + 0.0054\,(SO2)_t - 0.0019(O3)_t + 0.0007(TSP)_t \quad \text{.....(6)}$$

The relative risk estimates of asthma hospital admission, for unit increase, from the respective models (listed above), in relation to each pollutant level increment was calculated by exponentiation the beta coefficient included in the final four models, one for each season, and the confidence intervals (CI) were calculated using $e^{(\beta x \pm 1.96*SE)}$. Of all urban environmental pollutants in Halifax (see figure 2), CO shows consistently the highest statistically significant risk for asthma admissions, followed by NO_2 (except in the spring) and TSP levels (except in the spring). A delayed effect of up to lag 2 is seen in the fall CO levels and this was consistently noted elsewhere in the literature [45, 46]. O_3 is significant in the single pollutant models (results not shown here) when unadjusted for CO and this is due to confounding. This confounding effect is consistent with the literature [21, 47, 48]. NO_2 was included in the Canadian AQHI since it was found significant for asthma admissions in other Canadian studies [29, 49]. Our finding of NO_2 confounding with O_3 was also noted by other researchers [50]. Halifax TSP levels shows significant effects in all but spring seasons regardless of the presence or absence of other pollutants (figure 2). SO_2 levels are not significantly associated with asthma RR when adjusted for NO_2 and O_3 this is again possibly due to confounding as noted in the literature [51, 52]. With respect to above findings I suggest that the relative risk of each pollutant and the combination of pollutants that effect asthma admissions is subject to change seasonally for the urban pollutant site of Halifax. Moreover, of the combination of pollutants in NAQHI, only NO_2 found to play a significant role for asthma admission risk assessment for Halifax urban site.

The four final models for the Sydney (waste) site are listed below.

$$Winter: \log(\mu_t) = 0.086y_{t-1} + 1.2204(Pb)_{t-1} + 0.0004\,(PM10)_{t-2} + 0.0004(PM10)_{t-2} \quad \text{.....(7)}$$

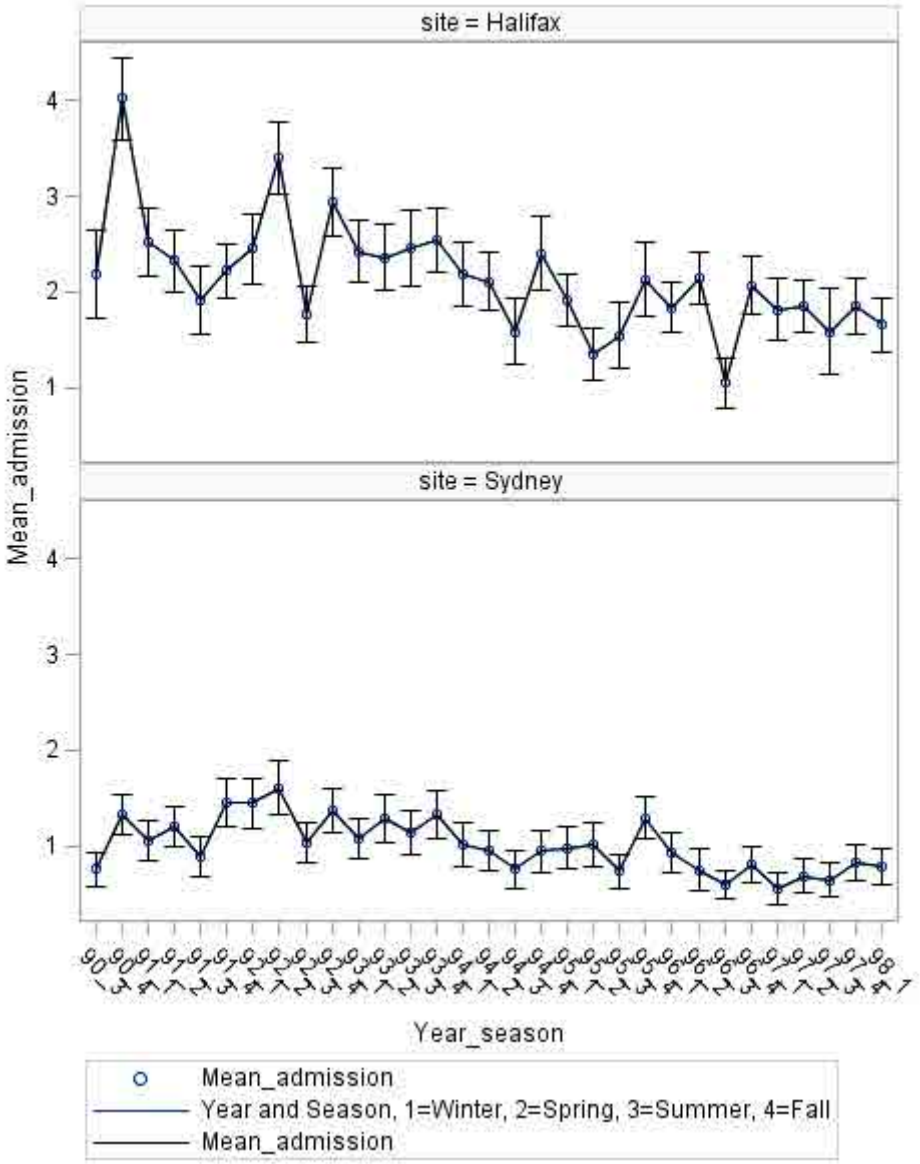
$$Spring: log(\mu_t) = 0.056y_{t-1} - 0.8218(Pb)_{t-1} + 1.0597\,(Pb)_{t-2} \quad \text{.....(8)}$$

$$Summer: log(\mu_t) = 0.171y_{t-1} + 1.1046(Pb)_t - 1.1598\,(Pb)_{t-1} + 0.0018(SO2)_t \quad \text{.....(9)}$$

$$Fall: log(\mu_t) = 0.040y_{t-1} - 0.0418(Pb)_t + 0.0005\,(PM10)_{t-2} + 0.0008(SO2)_t \quad \text{.....(10)}$$

Of all waste disposal environmental pollutants in Sydney (see figure 3), Pb shows consistently the highest significant risk for asthma. Delayed effects are seen in the winter, spring and summer seasons. In this waste disposal site, lead levels are prominent but TSP levels are redundant possibly because of confounding with Pb. Sydney PM_{10} levels are significant in the fall and winter seasons

FIGURE 1. Halifax and Sydney hospital admission (mean and CI) by year and season.

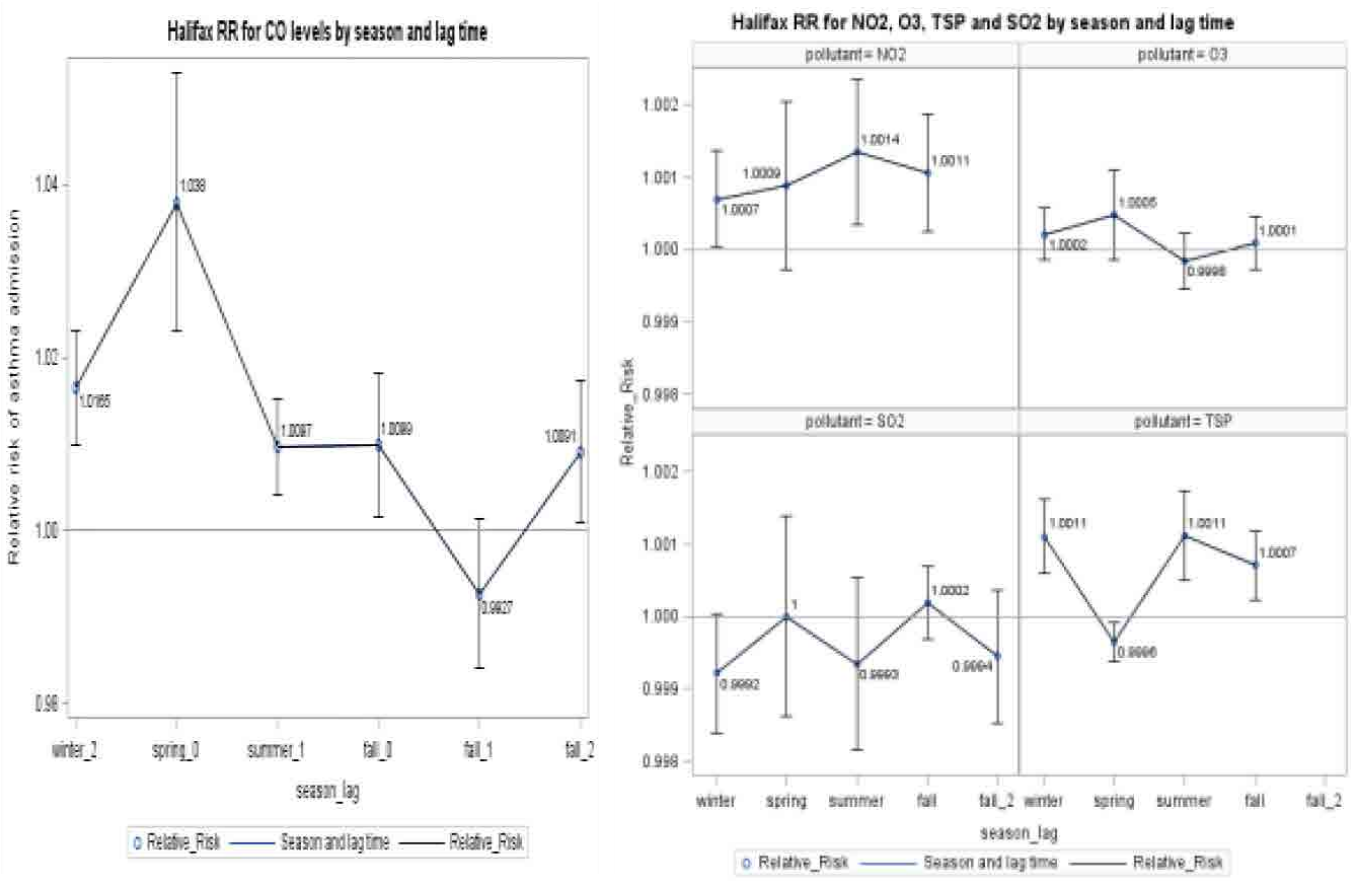


when adjusted for Pb (figure 3). In Sydney, particulates, including Pb are found to be contributing to increased risk of asthma admissions more than other pollutants. Sydney waste disposal pollutants also shows seasonal differences.

It is unlikely that a one unit increment of pollutant level provides a reasonable estimate of exposure risk and the researchers have used interquartile range (IQR) of pollution level increment to quantify risk [27, 28, 46]. To gain a better understanding of the pollutant risk, I incorporated pollution level variation by calculating the asthma admission risk for interquartile increment (see Table 1). In what follows the discussion is based on relative risk of asthma admissions for an IQR increment, $e^{\beta x IQR}$, confidence interval (CI) $e^{(\beta x IQR \pm 1.96 * SE x IQR)}$ of pollutant levels. Table 1 displays the IQR, RR and CI for each urban (Halifax) and waste disposal (Sydney) site specific exposure models where β coefficients are listed under the models equations 3-10. Note that each site, each multipollutant model variable is listed in the first column and the confounder listed in the last column indicates the variable which is significant in a marginal model but became insignificant when the main variable in the first column is added to the model. Marginal (single pollutant) model results are not shown here.

CO and NO_2 in the urban site and Pb in the waste site contributes statistically significantly to the highest asthma relative risk. Urban site pollution effects in different seasons are different from that of the waste disposal site seasonal effects for two of the common pollutants, TSP and SO_2, thereby indicating the importance of source and site specific analyses. The present study results show delayed effects up to lag 2 for CO, NO_2 in Halifax and for Pb and PM_{10} levels in Sydney and this result is consistent with other

FIGURE 2. Halifax Asthma relative risk for unit increase in pollutant level by season.



Note: Season_number indicates the lag time of the pollutant that was associated with asthma RR for the particular seasonal model

Canadian studies [53, 54]. However, longer lag effects for NO_2, SO_2 up to 4 days were found in other Canadian studies [53, 54] and in small areas it is not possible to assess longer lag effects due to data variation redundancy in multipollutant models.

The fitted models are assessed and then the estimates (Beta coefficients) are used in the air quality health index formation. From the findings Sydney models are far too sparse (data redundancy) and are solely driven by lead and other particulate levels. Due to low admissions in Sydney and lack of variations in the ambient pollutant levels most variables lack variation to provide model estimates and are noted as redundant (Table 1). Multi pollutant index formulation was only possible for Halifax estimates. Halifax model estimates are used for the goodness of fit and air quality health index assessments.

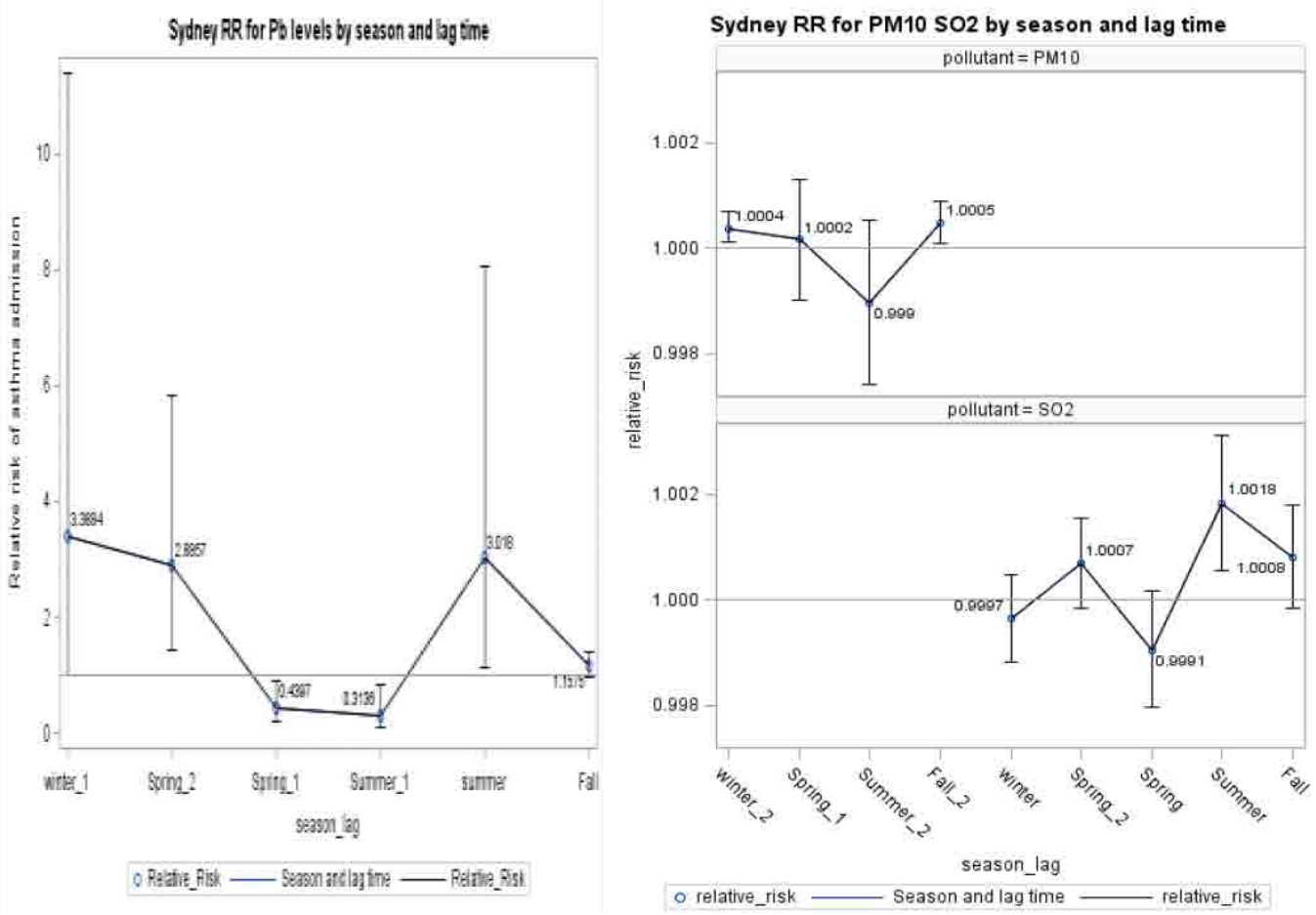
Goodness of fit based model assessment: Goodness of fit of the zero inflated, auto regressive seasonal multipollutant models presented in this paper, for Halifax (equations 3-6 above) is assessed first to assess goodness of fit to the actual data (appendix A, details and findings) and then to assess the significance of each of the specific data structures. Evidently, the models fitted reasonably well for zero and non-zero admissions. Next part of model evaluation is to compare model based asthma admission risk scores with NAQHI risk scores of the models fitted with and without CO and also set of models fitted with and without considering auto correlation and zero inflation.

Implications for asthma admission risk assessment: Comparison of model based index with NAQHI values

In this model evaluation, traditional AQHI parameters needed to be adjusted due to lack of PM data and this is done using a linear prediction of TSP levels and the relationship between TSP and PM was theoretically and practically justified in the literature [55, 56].

NAQHI used pooled weighted estimates across 11 national sites to formulate a national index and the details are in Stieb et al. (2008) [8]. For the purpose of comparison with model based estimates of this paper from a single Halifax site, I use the unscaled version of the NAQHI. Another change is that NAQHI was formulated based on single pollutant models beta coefficients and therefore scaled version includes exponentiation of each beta coefficient multiplied by the pollutant level and then

FIGURE 3. Sydney Asthma relative risk for unit increase in pollutant level by season.



Note: Season_number indicates the lag time of the pollutant that was associated with asthma RR for the particular seasonal model

subtracting 1 from each component. The model based index (MBI) in this paper is based on multipollutant models and therefore MBI is formed by multiplying exponents of a linear combination of beta coefficients multiplied by the pollutant level and then subtracting 1 to scale down to 0. Indices are listed below.

The unscaled version Canadian NAQHII, based on NO_2, PM_{10} and O_3 described in Stieb et al (2008) [8] is given by

$$NAQHI = ((e^{0.000871\times NO_2} - 1) + (e^{0.000531\times O_3} - 1) + (e^{0.000297\times PM_{10}} - 1))$$

The significant beta coefficients (see Table 1 for significance) from equations 3-6 above displayed for Halifax is used to formulate model based indices (MBI) risk scores for each season.

Present study model based index (MBI), with CO (MBI+CO) and without CO (MBI-CO) scored for each season is listed in Table 2 column 3 and 4. MBI with CO for winter is

$$MBI + CO = [(e^{\mathbf{0.0151}\times CO(t-2)})\times(e^{\mathbf{0.0007}\times NO_2})\times(e^{\mathbf{0.0011}\times TSP(t-1)})\times(e^{-\mathbf{0.0008}\times SO_2})] - 1$$

and without CO for winter was

$$MBI - CO = [(e^{\mathbf{0.0009}\times NO_2})\times(e^{-\mathbf{0.0004}\times O_3})\times(e^{\mathbf{0.0005}\times TSP(t-1)})\times(e^{\mathbf{0.00001}\times SO_2})] - 1$$

Daily NAQHI and two MBI (with and without CO) based asthma admission risk scores are calculated for each day based on each of the three indices for each season, formulated as above, using the beta coefficients, listed in the equations (3)-(6) and then multiplied by the respective ambient pollutant levels for each day of the season. Daily values are plotted in Figure 4 and the means and standard errors, aggregated for the season were calculated and are listed in Table 2. NAQHI scores are categorized by Environment Canada as low risk (category 1, below 3), moderate risk (category 2, 4-6) and high risk (category 3 from 7-10) [10, 20]. Percentage of days by each risk category are listed in Table 2 in each row second line. For example winter (97.6, 2.1, 0.28) for MBI+CO indicate the model estimated risk scores were 97.6% days with low risk, 2.10% days with moderate risk and 0.28% days with high risk scores. In order to understand the influence of zero inflation, four seasonal models are fitted to asthma admissions without considering zero inflation and the

TABLE 1. Adjusted relative risk of asthma admissions for IQR increments of pollutant levels.

Season/model	Pollutant	IQR	Relative Risk (RR) (95% CI)	Pollutant lag days	Confounder
Halifax (urban site) Winter (Model equation (3))	CO (ppm)	9.8	1.16 * (1.09-1.23)	2	O_3
	NO_2 (ppb)	211.8	1.16* (1.01-1.33)	0	SO_2, O_3
	SO_2(ppb)	214.8	0.84^{mns} (0.71-1.01)	0	O_3, NO_2
	TSP *(μg/m³)*	168.0	1.20* (1.11-1.31	1	None
	O_3 (ppb)	357.6	1.08^{ns} (0.95-1.23)	0	CO, NO_2
Halifax (Urban site) Spring (Model equation (4))	CO ppm	7.4	1.32* (1.18-1.47)	0	O_3
	NO_2 ppb	257	1.28^{ns} (0.95-1.74)	0	SO_2, O_3
	SO_2 ppb	244.5	1.001^{ns} (0.76,1.31)	0	O_3,NO_2
	O_3 ppb	326.4	0.89* (0.81-0.98)	1	CO, NO_2
	TSP *μg/m³*	156	1.08^{ns} (0.98-1.19)	1	none
Halifax (Urban site) Summer (Model equation (5))	CO ppm	10.6	1.11* (1.05-1.17)	1	O_3
	NO_2 ppb	210.8	1.33* (1.12-1.54)	2	SO_2, O_3
	SO_2 ppb	193.0	0.88^{ns} (0.65-1.11)	2	O_3, NO_2
	O_3 ppb	320.4	0.95^{ns} (0.83-1.08)	2	CO, NO_2
	TSP *μg/m³*	132	1.16* (1.08-1.24)	0	None
Halifax (Urban site) Fall (Model equation (6))	CO ppm	13.3	1.14* (1.02, 1.27) 0.91^{ns} (0.81, 1.02) 1.13* (1.01, 1.26)	0 1 2	O3
	NO_2 ppb	219	1.26*(1.05, 1.51)	2	SO_2, O_3
	SO_2 ppb	182.4	2.69^{ns} (0.31-23.54)	0	O_3, NO_2
	O_3 ppb	314.4	0.55^{ns} (0.03-9.83)	0	CO, NO_2
	TSP *μg/m³*	156	1.12* (1.04-1.20)	0	none
Sydney (waste site) winter (model equation 7)	Pb *μg/m³*	0.36	1.55*(1.003-2.40)	1	None
	PM_{10} *μg/m³*	192.0	1.08*(1.02-1.14)	2	Pb, TSP
	SO_2 ppb	81.0	Redundant	-	None
	TSP *μg/m³*	480.0	Redundant	-	PM_{10}
Sydney (waste site) Spring (model equation 8)	Pb *μg/m³*	0.36	1.46* (1.14-1.89)	2	PM_{10}
	SO_2 ppb	41.7	Redundant	-	None
	TSP	456.0	Redundant	-	None
	PM_{10} *μg/m³*	120.0	Redundant	-	None
Sydney (waste site) Summer (model equation (9))	Pb *μg/m³*	0.24	1.30*(1.03-1.65)	0	None
	SO_2 ppb	33.26	1.13*(1.04-1.22)	2	None
	TSP *μg/m³*	258.0	Redundant	–	None
	PM_{10} *μg/m³*	168.0	Redundant	–	Pb
Sydney (waste site) Fall (model equation (10))	Pb *μg/m³*	0.24	0.99^{ns} (0.94-1.06)	0	PM_{10}
	PM_{10} *μg/m³*	156	1.08* (1.01-1.15)	2	Pb
	SO_2 ppb	57.4	1.05^{ns} (0.99-1.11)	0	PM_{10}
	TSP *μg/m³*	432.0	Redundant	–	None

**Highly significant, mns =marginally non-significant, ns=non-signficant; lag days=0 for same day admissions*
Confounder = Significant in the marginal model and insignificant when the confounder is added to the model

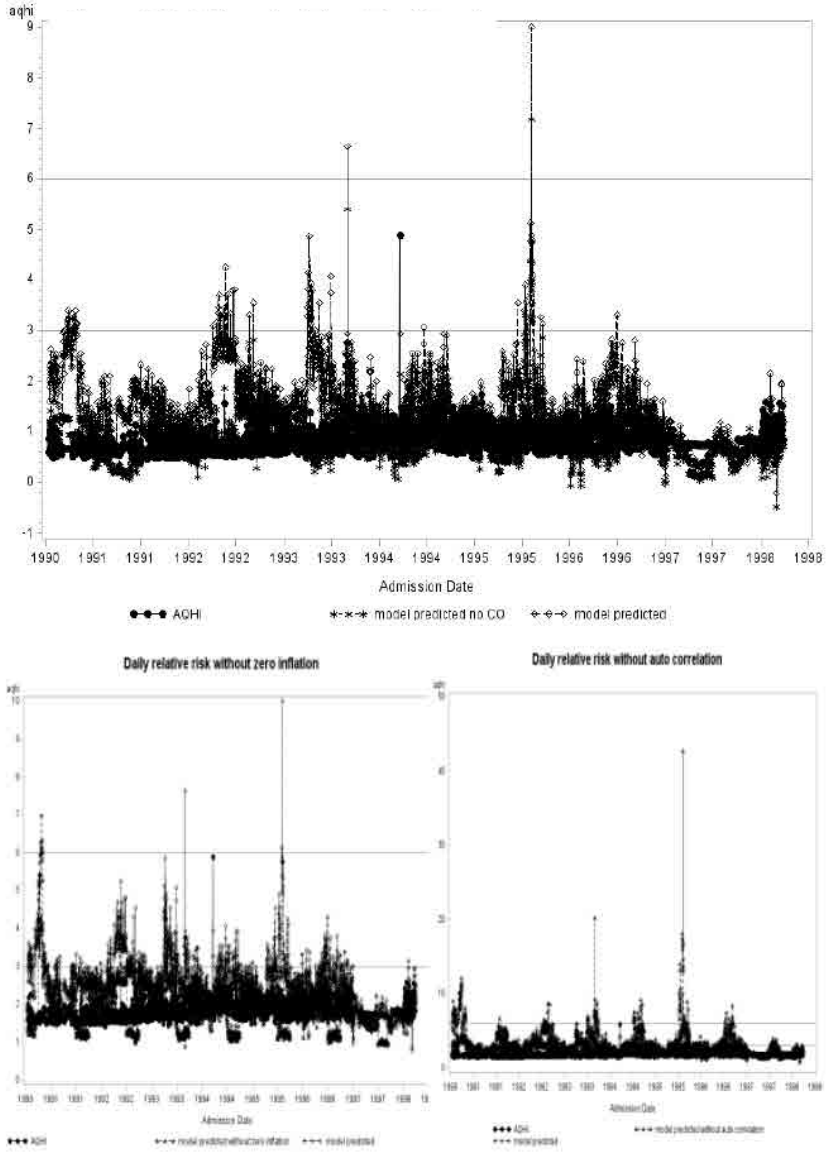
corresponding risk scores are listed in column 5 of Table 2 and the values are plotted in Figure 4 lower left panel. Another four models are fitted without autocorrelation and the model resulting scores are plotted in Figure 4 lower right panel and the risk scores are summarized in column 6. Model based indices (MBI+CO, MBI-CO without

TABLE 2. Mean measures of Canadian air quality index, model predicted index with and without CO levels for Halifax (rescaled 1-10).

Season	Index based mean + SE for each season and (% days in risk category) with significance				
	NAQHI	MBI+CO	MBI-CO	MBI+CO, no zero inflation	MBI+Co without AR
Winter	(1.87+0.01) (99.9, 0,0.1)	(2.01+0.01) (97.6,2.1,0.28)	(1.69+0.01) (99.9,0.14,0)	(2.02+0.01) (98.5,1.3,0.3)	2.20+0.02 (96.7,2.9,0.4)
Spring	(1.86+0.01) (100,0,0)	(2.37+0.02) (60.1,34.5,5.3)	(1.57+0.01) (100,0,0)	(2.22+0.02) (97.3,2.7,0)	2.74+0.03 (70.8,25.9,3.3)
Summer	(1.81+0.01) (99.9,0.1,0)	(2.46+0.02) (73.7,22.0,4.3)	(2.26+0.02) (93.5,4.7,1.8)	(1.23+0.01) (100,0,0)	5.16+0.10 (9.3,20.5,70.3)
Fall	(1.82+0.01) (100,0,0)	(2.05+0.02) (93.1,5.3,1.6)	(1.93+0.01) (99.7,0.3,0)	(2.58+0.03) (90.4,5.4,4.2)	2.96+0.03 (63.9,31.3,4.9)
P value	0.445	0.0001	0.0001	0.0001	0.0001

p-value for chi square test of independence between season and risk category 1=low, 2-moderete and 3=high.

FIGURE 4. Model based relative risk with and without CO, auto correlation and zero inflation- comparison with aqhi based relative risk



zero inflation and without auto correlation) are developed based on asthma hospital admissions and therefore the estimates listed in Table 2 correspond to asthma admission relative risk.

According to the results shown in figure 4 and Table 2, the Canadian NAQHI underestimates the Halifax, urban pollution based asthma admission risk. This is in an area where CO showed highly significant effect on asthma admissions. In terms of risk categorization NAQHI would categorize as no risk in all seasons and the MBI+CO would categorize as 34.5% and22% days as moderate risk for spring and summer seasons respectively. More over NAQHI would miss 5.3% and 4.3% high risk days in the spring and summer seasons respectively. Without CO the risk is lower and closer to NAQHI based risk. Zero inflated models estimate the effect of having any admission and exclusion of zero inflation seriously underestimates the asthma risk (Table 2, Figure 4). Zero inflated models estimate the effect of having any admission and the zero inflation part of this study is mostly accounted by the week day and temperature variations. Clearly, the zero inflation effects are prominent in the spring and summer seasons, during which time a clear underestimation is displayed without zero models (figure 4, Table 2). Asthma admission time series are auto correlated and the fitted models with and without autocorrelation show significant differences. There are serious overestimation, especially in the summer and fall seasons, when autocorrelation is ignored. Autocorrelation, makes the lower values staying lower and higher values staying higher. Overestimation is higher in warmer seasons, summer and fall, where the autocorrelation is larger than the cooler seasons of winter and spring. Moreover, no zero inflation model based risk scores without auto correlation (AR part) certainly provide significantly different risk scores. This indicates that the use of NAQHI for Halifax asthma admission risk assessment is problematic without incorporation of local level estimates that are coming from complex models particularly suited to complex data structures. Another significant feature of the local indices is inclusion of delayed effects, which were ignored in NAQHI.

These results suggest that the risk of asthma admissions is highly sensitive to local level pollutant combination effects that vary by season. There are few Canadian studies that have explored AQHI and asthma admissions and the lowest AQHI was found in the fall season (3.18+1.19) and the highest (3.2+0.02) was recorded for summer [10,11]. Congruent with the literature, the highest value in the present model is also in the fall (Table 2).

CONCLUSION

The findings of this paper suggest that the complex model fitting introduced herein enable accurate prediction of asthma hospital admission relative risk. In Canada NAQHI is recommended to provide advice to patients by family physicians [4]. Though two other Canadian city based studies [10, 11] found NAQHI as a good predictor of asthma admission risk evaluation, the model based estimates of this paper prove the opposite. The researchers who formulated NAQHI found that the mortality based NAQHI as having weak correlation with hospital admissions. I find the Canadian NAQHI seriously underestimates Halifax fall asthma admission risk with sparse (zero admissions) data and therefore stresses the importance of using an index that includes CO levels for urban small city specific air quality health risk assessment and also to use a model that fits well with site specific complex data structures. Even the model without CO provided lesser AIC indicating that the site specific indices provide accurate predictions. Lead is a prominent contributor in waste disposal site asthma risk.

This study has several limitations. Ecological time series studies have limitations that assume ambient exposure is homogeneous across all genders, age groups and areas. Besides methodological complexity, the present study findings indicates that it is vital to include local level, ambient air pollution data structure specific modeling in estimating asthma morbidity health risk. Further it is revealed the importance of consideration of season specific models that incorporate zero inflation and auto correlation in the estimation and risk assessment even when the average ambient pollution levels are below the specific standards.

APPENDIX A: GOODNESS OF FIT OF THE MODEL

The whole model goodness of fit was assessed, by comparing the model estimated probabilities based asthma admissions with actual asthma admissions for each season for Halifax. Using the model (3-6 equations) based probabilities for x number of admissions (x=1, 2,…11) was calculated by multiplying the total number of days. Note that zero admission days were calculated using zero inflated models (not shown here). Chi-square goodness of fit statistics $=\frac{(actual-estiamted)^2}{estimated}$ follows 10 degrees of freedom and the chi-square probability $p > 0.05$ indicated a significant goodness of fit.

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