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Acute Effects of Outdoor Air Pollution on FEV_1: A Panel Study of Schoolchildren with Asthma

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Abbreviations:

AIC -Akaike's information criterion

IQR - interquartile range

FEV_1 - one-second forced expiratory volume

NAPS - National Air Pollution Monitoring System

NO_2 - nitrogen dioxide

O_3 - ozone

PEF – Peak expiratory flows

$PM_{2.5}$ - fine particulate matter

SO_2 - sulfur dioxide

ABSTRACT

Background: Urban air pollution has been associated with morbidity but little information exists on how it affects diurnal variation of lung function in children with asthma.

Objective: To investigate the acute effects of traffic-related pollution on lung function among children with asthma.

Methods: We recorded morning and evening FEV_1 for 28 consecutive days in 182 elementary schoolchildren with physician-diagnosed asthma, and monitored ambient hourly air pollution concentrations.

Results: An interquartile (IQR) increase (6.0 $\mu g/m^3$) in the previous 24-hr (2000Hr to 2000Hr) mean concentration of fine particulate matter ($PM_{2.5}$) was associated with a 0.54% (95% CI 0.06,1.02) decrease in bedtime FEV_1, p=0.027. This association persisted in two-pollutant models with ozone, nitrogen dioxide, and sulphur dioxide. An interquartile increase in mean daytime (8 a.m. to 8 p.m.) $PM_{2.5}$ of 6.5 $\mu g/m^3$ was associated with a 0.73% (95% CI 0.10,1.37) decrease in FEV_1 over the course of the day expressed as 100*(FEV_1 bedtime - FEV_1 morning)/ FEV_1 morning, p=0.024.

Conclusions: This study suggests that in children with asthma, relatively low concentrations of urban air pollution worsen lung function over a short period of time, even within a day. Of the pollutants measured, $PM_{2.5}$ appears to be the most important.

Keywords - air pollution, children, environment, lung function

INTRODUCTION

Acute and chronic exposure to urban air pollution in North America and Europe has been associated with increased respiratory symptoms, reduced lung function, hospitalizations, and death from respiratory diseases [1-5]. Although many different study designs have been used, the majority of evidence comes from comparisons of daily concentrations of air pollutants with daily mortality or hospital admission counts. There have also been several panel studies which have reported associations between daily symptoms and/or lung function to daily measures of various air pollutants [6-14]. The present study focuses on acute changes in lung function. We studied not only the effects of between-day changes in air pollution but also we also tested a relatively unique hypothesis that acute change in lung function within a day, between morning and evening (diurnal change) was associated with fine particulate concentrations on the same day.

METHODS:

Study population: The study was carried out in Windsor Ontario, Canada, with a population of 332,300 based on intercensal interpolation estimates (http://hc-sc.gc.ca/). A unique aspect of the city is the Ambassador Bridge which carries several thousand trucks daily between Windsor and Detroit, Michigan, USA. We identified children with asthma from a questionnaire survey done in the previous year of approximately 16,000 elementary schoolchildren in Windsor. For the present study, we selected children whose parent or guardian had given a positive response to: 'Has a physician ever told you this child had asthma' and who had agreed to be contacted about future research. We selected children who were between the ages of 9 and 14 years when the initial questionnaires were completed, spoke either of Canada's official languages (English or French), and lived in homes without cigarette smoke. A list of all eligible children satisfying these criteria was constructed. We telephoned their homes in random order and recruited the first 182 subjects who agreed to participate. The number of respiratory therapists available in Windsor to work on this study limited the number of subjects who could participate. The parent or guardian of each child gave written informed consent prior to having their child participate in the study. The study protocol was approved by the Research Ethics Board of Health Canada.

Study design: A short-term longitudinal study design with repeated measures was used. Each child completed a daily symptom diary, and performed forced expiratory flows in the morning and at bedtime for 28 consecutive days. Due to resource constraints, children were studied in one of two test periods: October 11 to November 7, or November 14 to December 11, 2005.

Air Pollution Measurements: City-wide air pollution hourly levels were estimated by averaging measures from two fixed-site monitors located in the western area of the city, upwind from the prevailing winds. These monitors, part of Environment Canada's National Air Pollution

Monitoring System (NAPS) provided ambient levels of hourly fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), ozone (O_3) and sulfur dioxide (SO_2). The majority of the population lived within 10km downwind.

Forced expiratory volume in one second: Respiratory therapists instructed parents and children on the use of hand-held flow meters and daily symptom diaries. FEV_1 was estimated using a PiKo-1® electronic flow PEF/FEV_1 meter (Ferraris Medical, Louiseville, CO, USA). Three flows were to be recorded twice each day, first thing on arising in the morning and again at bedtime, before taking breathing medications. For analyses we used the maximum evening and morning FEV_1 value expressed as a percentage of predicted based on the equations derived by Hankinson et al.[15]. We also analysed the diurnal (within-day) variation in lung function was expressed as 100*(FEV_1 bedtime - FEV_1 morning)/FEV_1 morning.

STATISTICAL ANALYSES

All statistical analyses were performed using the SAS software package (SAS Institute. SAS Version 9.1. Cary, NC, U.S.A). Differences in the distribution of children's characteristics between the two study periods were evaluated using the Chi-Square test statistic. Daily mean concentrations of the ambient pollutants as well as temperature and relative humidity were calculated, and Pearson correlation coefficients were estimated to better understand their interrelationships.

To estimate the mean pollution values twelve and twenty-four hours prior to the FEV_1, measurement, we assumed that, on average, morning FEV_1 was performed at approximately 8 a.m. and bedtime testing at 8 p.m. To evaluate temporal associations between ambient levels of air pollution and FEV_1, we calculated the mean of hourly air pollution measures for the following periods preceding the FEV_1 measure: <12 hours, 12 to < 24 hours, and 0- 24 hours. A similar approach was used to create temporal metrics for temperature and relative humidity.

The results obtained from linear mixed models were expressed as the percent change in median FEV_1 corresponding to an increase in the interquartile range (IQR) in air pollutant levels. The use of the IQR serves to standardize each pollutant facilitating comparisons between the magnitude of effect of different pollutants [16]. We employed an autoregressive covariance structure (AR1), which allows for a greater within-subject autocorrelation for FEV_1 measures taken more closely in time. We assumed a random intercept and a fixed slope. There were no statistically significant differences in the fit of the models using fixed compared to random slopes.

The same approach was used to control for confounding in the logistic and linear mixed model. We adjusted symptoms and $FEV_1$for all variables in Table 1 that were associated at a level of significance of $p \leq 0.15$ with both ambient measures of air pollution and FEV_1. This list of potential confounders included: the daily mean temperature, relative humidity, day of the week, number of hours spend on outdoor activities (<2, ≥2 hours), sex, and study period. Two pollutant models were fit to characterize which pollutant was more strongly associated with FEV_1 after adjusting for effects of other correlated ambient measures.

RESULTS

Characteristics of the participants are shown in Table 1. During the first period of enrolment, a smaller percentage of participants were female (30.5%) relative to the second period (44.8%; $p< 0.05$). Overall, 58.8% of children's households were reported as having a household pet. To be included in the study, all subjects had a history of 'ever had asthma', and most (95.1%) reported that they still had asthma. 96.7% reported at least one respiratory symptom during the 28 day study period, but 42.3% did not report taking any asthma medication during this same time. On average, children in the first study group reported a mean of 2.2 hours outside daily compared to 1.6 hours in the second group ($p<0.0001$).

For each child, we calculated the morning and bedtime percent predicted FEV_1 averaged over their 28 days of study (Table 2). The median values for both these measures were similar to the mean values (<2%) consistent with a near normal distribution. The diurnal change in FEV_1 from morning to evening, expressed as 100*(FEV_1 bedtime - FEV_1 morning,)/FEV_1 morning was 2.3% whereas the median change was only 0.4% with an interquartile range of 0.4 to 7.6. We assessed the effect of time on lung function to determine if there was evidence of a learning effect. The variables; time (number of days each subject was studied), study period (October-November, November-December), and time*study period were not significantly associated with FEV_1 (all p-values greater than 0.2).

Concentrations of air pollutants and interquartile ranges were well below the US EPA ambient air quality guidelines for $PM_{2.5}$ of 35 $\mu g/m^3$ for a 24-hr average and 15 $\mu g/m^3$ for an annual average (http://epa.gov/particles/pdfs/20060921_factsheet.pdf). In the present study, the 24-hr mean was 7.8 ug/m^3 and the interquartile range was 6.0 ug/m^3 (Table 3). Ozone decreased, SO_2 increased, and $PM_{2.5}$ remained stable over the study period (Figure 1).

SO_2, NO_2, and $PM_{2.5}$ were positively correlated with each other whereas ozone was negatively correlated with these three pollutants (Table 4). The strongest correlation between two

pollutants was 0.68 ($p<0.0001$) observed with NO_2, and $PM_{2.5}$.

Bedtime FEV_1. Adjusted for daily mean temperature and relative humidity, day-of-week, duration of outdoor activity, sex, and study period, an interquartile (IQR) increase (6.0 $\mu g/m^3$) in the previous 24-hr (2000Hr to 2000Hr) mean concentration of $PM_{2.5}$ was associated with a 0.54% (95% CI 0.06,1.02) decrease in bedtime percentage of predicted FEV_1, p=0.03 (Table 5). No statistically significant associations were found between bedtime FEV_1 and prior $PM_{2.5}$ concentrations averaged 24 to 48 hours, 0 to 48 hours, or 0 to 72 hours before lung function was measured. We found no statistically significant associations between evening FEV_1, and NO_2, SO_2 and ozone In two-pollutant models with SO_2, NO_2, or O_3, the $PM_{2.5}$ effect remained significant at $p<0.05$ (Figure 2).

Morning FEV_1. We found no associations between morning percentage of predicted $FEV_1$and pollutant concentrations with averaging times of 0800Hr the day prior to 0800Hr on the test day, 2000 Hr to 0800Hr, and 2400Hr to 0800Hr (overnight period). For the latter, adjusted mean interquartile increases in air pollution were associated with changes of 0.41 (95%CI -0.18, 0.99) for SO_2, 0.09 (95%CI -0.25,0.43) for NO_2, -0.17 (95%CI -0.69,0.35) for O_3, and 0.28 (-0.12,0.68) for $PM_{2.5}$.

Diurnal change in FEV_1. An interquartile increase in daytime $PM_{2.5}$ (6.5 $\mu g/m^3$) averaged between (0800Hr to 20000Hr) was associated with a 0.73% (95% CI 0.10, 1.37) decrease in diurnal FEV_1 change, expressed as 100*(FEV_1 bedtime - FEV_1 morning)/ FEV_1 morning, p=0.024 (Table 6). No statistically significant association was found between diurnal FEV_1 and $PM_{2.5}$ concentrations averaged 24 to 48 hours, 0 to 48 hours, or 0 to 72 hours before lung function was measured. Diurnal declines in FEV_1 during the daytime were also associated with increases in daytime NO_2 (p=0.024) and SO_2 (0.036) (Table 6). In two-pollutant models with SO_2, NO_2, or O_3, the $PM_{2.5}$ effect remained statistically significant (p=0.016) only with O_3 (Figure 3).

Effect modification of the FEV_1 response to air pollutants. For the association between FEV_1 and $PM_{2.5}$, the first order interaction term for corticosteroid use (on at least 50% of the study days v. less) was not significant but power was poor with only thirty-five subjects reporting corticosteroids on at least half of the days. No significant differences in the FEV_1 - pollutant association were found for any of the pollutants and the following groups: male v. female subjects, those who spent at least two hours outdoors daily v. those who spent less, and those whose baseline FEV_1 was less than 85% v. at least 85%. For the gender comparison, the percent-predicted change in FEV_1 for an interquartile change in 24 hour mean $PM_{2.5}$ was -0.54 (95%CI -1.13, 0.04) for males and -0.54 (95%CI -1.37, 0.28) for females. For baseline FEV_1 level, the percent-predicted change in $FEV_1$was -0.88 (95%CI -1.53, -0.22) in the group with FEV_1 at least 85% and -0.19 (95%CI -0.89, 0.52) in those with lower FEV_1.

Other response variables. The presence or absence of difficulty breathing, cough, wheeze, and chest tightness was indicated on the daily diary. The odds ratio for reporting chest tightness was 1.30 (1.06 - 1.58) for days with a mean SO_2 in the greatest quartile ($\geq$ 8.8 ppb) v. the lowest quartile (<2.3 ppb). No other similar contrasts between air pollutants and symptoms were significant at a p-value of <0.05. We did not find any significant effects of air pollutants on the peak expiratory flow measures but all point estimates were negative. For an interquartile increase in 24 hour mean $PM_{2.5}$, percent predicted peak flow decreased by -0.17 (95%CI -0.70,0.35).

DISCUSSION

Key findings. Among children with a history of asthma, bedtime lung function decreased with increased ambient concentrations of $PM_{2.5}$ even after adjustment for other pollutants. There was an approximate half-percent decline in the percentage of predicted FEV_1 for an interquartile increase in pollutant. FEV_1declines were associated with recent air pollution exposure, both the 24- hour average prior to bedtime flows, and also the 12 hour average during the day. Others have detected minimal or no effects within the past 24 hours although significant effects were detected from five-day averaged particulate concentrations [9];[13]. Although both $PM_{2.5}$ and NO_2 may represent mobile combustion-related air pollution, two-pollutant models indicated that $PM_{2.5}$ had the most robust effect on lung function. The air pollution concentrations in Windsor were much lower than many large U.S. cities where particulate pollution has been associated with mortality [4]. We observed decreases in lung function at 24-hour $PM_{2.5}$ concentrations approximately five times less than the U.S. National Air Quality standard of $35\mu g/m^3$.

Significance of Findings. We were able to detect an adverse biological effect on the lungs from air pollution at levels within currently accepted guidelines for public safety, suggesting that air pollution standards should be revisited. Although the FEV1 change during a clinically diagnosed asthma exacerbation is much larger than the 0.54% change observed in this study, the latter is of public health importance. All children in the community are exposed to the ambient air pollution, resulting in a large number of children affected. Assuming that there is a population distribution of asthma severity and of sensitivity to air pollution, children with severe disease and increased susceptibility to air pollution would be more likely to have a clinically important exacerbation of asthma on high air pollution days. This argument is supported by the empiric evidence. Norris et

al reported that a change in daily $PM_{2.5}$ of 11 ug/m^3 was associated with a relative risk estimate of 1.15 (95% CI 1.08,1.23) for a visit to the emergency department for asthma [17]

Strengths and limitations of the present study. We did not have objective measurements of asthma. The use of medication would be more likely among those with more severe asthma, but reported use was not an effect modifier, suggesting that asthma severity is not a determinant of the response to air pollution. A meta-analysis of air pollution studies in children did not find children with asthma to more susceptible than children without diagnosed asthma which also suggests that asthma severity is not a consistent effect modifier [18]. We do not know the reason for the stronger association between air pollution and bedtime flows compared to morning flows. Perhaps the children's air pollution 'dose' would be less in the 12 hours before the morning FEV_1measure because they would be indoors and exposed to lower concentrations of ambient pollution. Also minute ventilation would be less while sleeping than during wakefulness. We did not measure indoor air quality but only children living in smoke-free homes were included. Associations between FEV_1 and day-to-day changes in ambient air pollution would not be confounded by indoor air allergens or irritants unless they changed day-to-day in concert with outdoor air pollution. Janssen et al [19] studied the association between personal and outdoor concentrations of PM_{10} over time among 37 non-smokers. The median Pearson correlation coefficient was 0.71 when not exposed to passive smoke indicating that changes in outdoor levels reflect changes indoors. The forced vital capacity manoeuvre required for the FEV_1 measurement was observed only during the training period. Increased variability of the test could have reduced the power to detect a true association with air pollution. However, we did detect an adverse relation with particles. The Pearson correlation coefficient between morning and evening values was $r=0.82$ $p<0.0001$) indicating a moderate degree of reproducibility.

Comparison of the present results with previous panel studies of children with asthma. Peters et al [13] studied a panel of 82 Czech children with asthma between November 1991 and February 1992. An increase of 6.5 mg/m^3 in five-day mean sulphate was associated with a 5.62 (95% CI -9.93,-1.30) litre/minute decrease in peak flow. Another report of the Czech panel by Peters et al [13] reported significant associations between air pollution and peak flow during September 1991 and March 1992. Mortimer et al [10] also detected a negative association between ambient ozone and morning peak flow among 846 children with a history of asthma recruited from eight U.S. urban centers. Peak flow decreased 0.59% (95% CI 0.13, 1.05) for each 15 ppb increase in the five-day moving average for ozone In one panel study of 22 Hispanic children with asthma by Delfino et al [8], peak flows were not found to be associated with ambient ozone, NO_2 or SO_2. In another panel of 19 children with asthma by the same lead investigator, a 0.7% (95% CI -1.9, 0.4) decrease in FEV_1 was associated with a 7.5 ug/m^3 increase in $PM_{2.5}$ averaged over the preceding 24 hours at a central site [9]. Using a passive nephelometer for personal monitoring, the observed effect size was statistically significant with a -5.9% (95% CI -10.8, -1.0) change in FEV_1 for a 30 ug/m^3 change. Multi-day moving averages for $PM_{2.5}$ resulted in larger effect sizes but these were not significantly different than for the previous 24-hr average. In our study, earlier changes were detected with significant effects seen between morning and evening lung function associated with same day $PM_{2.5}$. The effect size per ug/m^3 of $PM_{2.5}$ in our study was 0.08%, in close agreement with the 0.09% estimated in the study by Delfino et al [9] despite the mean $PM_{2.5}$ during the studies being 7.8 ug/m^3 and 10.3 ug/m^3 respectively. Whether exposed to higher or lower daily average concentrations of $PM_{2.5}$, it appears that equivalent changes in $PM_{2.5}$ have a similar magnitude of effect on lung function. Trenga et al [14] reported an adverse effect of centrally monitored $PM_{2.5}$ on the one-second forced expiratory volume of children with asthma, only if they were not receiving anti-inflammatory medications. We did not detect a significant difference between those with and

without asthma medications. A study similar to ours took place in Detroit, Michigan, which is connected to Windsor by the international Ambassador Bridge [20]. During six periods, each of fourteen days, 86 children performed FEV_1 measured using a portable device, and recorded daily $PM_{2.5}$, PM_{10}, and ozone. For the entire study group, no significant associations were reported between FEV_1 and pollutants. Subgroup analyses restricted to those reporting maintenance inhaled corticosteroids, and using three different lags, revealed 4 of 24 associations tested were statistically significant between single pollutants and diurnal FEV_1 variation and/or lowest daily FEV_1. For the subgroup reporting upper respiratory symptoms, 8 of 24 associations with single pollutants were positive at $p \leq 0.05$. The air pollutant association with diurnal variation was positive whereas it was inverse in our study. Whether or not an increase or decrease in diurnal variation is considered an adverse response depends on the reason. In our study, the morning flows did not change significantly with air pollution. Thus, the decreased diurnal variation was due to a smaller than expected FEV_1 improvement that normally occurs during the day unrelated to air pollution. A more recent study also compared air pollution levels to self-administered spirometry in a panel of children [21]. Fifty three subjects with asthma were studied for ten days. Peak hourly personal $PM_{2.5}$ (averaging 90$\mu g/m^3$) but not ambient levels, were associated with decreased FEV_1. Maximum morning FEV_1 decreases were seen with approximate eight-hour lags, and maximum afternoon and evening decreases were associated with twenty-four hour lags. No air pollution effects were seen in a group of sixteen children taking a beta-agonist, theophylline, and/or an anti-cholinergic medication. In our study, with much lower concentrations of ambient $PM_{2.5}$ but ten times the number of person-days of observation, we found maximum FEV_1 effects within a lag time of twenty-four hours after exposure and also effects on diurnal variation within a twelve hour period.

In summary, this study provides evidence that acute changes in urban air pollution, even within a day, at concentrations less than many North American urban centers, worsens lung function in children with asthma.

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Reference List

1. Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society. Bascom R, Bromberg PA, Costa DA, Devlin R, Dockery DW, Frampton MW. Health effects of outdoor air pollution. *Am J Respir Crit Care Med* 1996;153:3-50.

2. Brunekreef B, Holgate ST. Air pollution and health. *Lancet* 2002; 360:1233-1242.

3. Dockery DW, Pope CA, III. Outdoor Particulates. *In*: Steenland K, Savitz DA, eds. *Topics in environmental epidemiology*. New York: Oxford University Press, 2002; 119-166.

4. Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. Fine Particulate Air Pollution and Mortality in 20 U.S. Cities 1987-1994. *N Eng J Med* 2000; 343:1742-1749.

5. Stieb DM, Judek S, Burnett RT. Meta-analysis of time-series studies of air pollution and morality: effects of gases and particles and the influence of cause of death, age, and season. *J Air & Waste Manage Assoc* 2002; 52:470-484.

6. Chan CC, Wu TH. Effects of ambient ozone exposure on mail carriers' peak expiratory flow rates. *Environ Health Perspect* 2005;113:735-738.

7. Delfino RJ. Association of Asthma Symptoms with Peak Particulate Air Pollution and Effect Modification by Anti-Inflammatory Medication Use. *Environ Health Perspect* 2002; 110:A607-A617.

8. Delfino RJ, Gong H Jr, Linn WS, Pellizzari ED, Hu Y. Asthma Symptoms in Hispanic Children and Daily Ambient Exposures to Toxic and Criteria Air Pollutants. *Environ Health Perspect* 2003; 111:647-656.

9. Delfino RJ, Penelope JEQ, Floro J, Gastanaga VM, Samimi BS, Kleinman MT. Liu LJ, Bufalino C, Wu CF, McLaren CE. Association of FEV_1 in Asthmatic Children with Personal and Microenvironmental Exposure to Airborne Particulate Matter. *Environ Health Perspect* 2004; 112:932-941.

10. Mortimer KM, Neas LM, Dockery DW, Redline S, Tager IB. The effect of air pollution on inner-city children with asthma. *Eur Respir J* 2002;19:699-705.

11. Ostro B, Lipsett M, Mann J, Braxton-Owens H, White M. Air Pollution and Exacerbation of Asthma in African-American Children in Los Angeles. *Epidemiology* 2001;12:200-208.

12. Peters A, Dockery DW, Heinrich J, Wichmann HE. Medication use modifies the health effects of particulate sulphate air pollution in children with asthma. *Environ Health Perspect* 1997;105:430-435.

13. Peters A, Dockery DW, Heinrich J, Wichmann HE. Short-term effects of particulate air pollution on respiratory morbidity in asthmatic children. *Eur Respir J* 1997;10:872-879.

14. Trenga CA, Sullivan JH, Schildcrout JS, Shepherd KP, Shapiro GG, Liu LJ, Kaufman JD, Koenig JQ. Effect of particulate air pollution on lung function in adult and pediatric subjects in a Seattle panel study. *Chest* 2006; 129:1614-1622.

15. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med* 1999;159:179-187.

16. Lipfert FW, Wyzga RE. Statistical considerations in determining the health significance of constituents of airborne particulate matter. *J Air & Waste Manage Assoc* 1999; 49:182-191.

17. Norris G, Young Pong SN, Koenig JQ, Larson TV, Sheppard L, Stout JW. An association between fine particles and asthma emergency department visits for children in Seattle. Environ Health Perspect. 1999;107(6): 489–493.

18. Ward DJ, Ayres JG. Particulate air pollution and panel studies in children: a systematic review. *Occup Environ Med* 2004;61:e13

19. Janssen NA, Hoek G, Brunekreef B, Harssema H, Menswik I, Zuidhof A. Personal sampling of particles in adults: relation among personal, indoor, and outdoor air concentrations. *Am J Epidemiol* 1998;147(6): 537-547.

20. Lewis TC, Robins TG, Dvonch JT, Keeler GJ, Yip FY, Mentz GB, Lin X, Parker EA, Israel BA, Gonzalez L, Hill Y. Air Pollution-Associated Changes in Lung Function among Asthmatic Children in Detroit. *Environ Health Perspect* 2005;113:1068-1075.

21. Delfino RJ, Staimer N, Tjoa T, Gillen D, Kleinman MT, Sioutas C, Cooper D. Personal and Ambient Air Pollution Exposures and Lung Function Decrements in Children with Asthma . *Environ Health Perspect* 2008;116: 550-558.

Table 1: Selected characteristics of the 182 children participants by study period in Windsor, 2005

Characteristics	Oct 11-Nov 7 Number	%	Nov14-Dec11 Number	%	Overall Number	%	p-value *
Age (years)							
9-10	16	16.8	8	9.2	24	13.2	0.39
11	20	21.1	26	29.9	46	25.3	
12	26	27.4	33	37.9	59	32.4	
13-14	33	34.7	20	23	53	29.1	
Sex , female	29	30.5	39	44.8	68	37.4	0.05
Race, Caucasian	83	87.4	77	88.5	160	87.9	0.79
Household pets, yes	53	55.8	54	62.1	107	58.8	0.66
Currently have asthma , yes	90	94.7	83	95.4	173	95.1	0.84
Respiratory symptoms during the study period							
None	5	5.3	1	1.1	6	3.3	0.20
Breathing	62	65.3	64	73.6	126	69.2	0.44
Chest tight	52	54.7	57	65.5	109	59.9	0.27
Cough	84	88.4	83	95.4	167	91.8	0.20
Wheeze	56	58.9	59	67.8	115	63.2	0.38
Medication use during the study period							
Inhaled corticosteroid	36	37.9	32	36.8	68	37.4	0.88
Short acting β_2 agonist	33	34.7	31	35.6	64	35.2	0.90
Other asthma medication	20	21.1	13	14.9	33	18.1	0.29
No asthma medication	39	41.1	38	43.7	77	42.3	0.44
Total house income (CDN$)							
< 35,000	10	10.5	7	8	17	9.3	0.95
35, 000 – 80,000	25	26.3	23	26.4	48	26.4	
>80,000	24	25.3	22	25.3	46	25.3	
Unknown	36	37.9	35	40.2	71	39	
Daily outdoor activity, $\geq$ 2 hours	53	55.8	23	26.4	76	41.8	0.00
Weight (kg)							
< 39	29	30.5	23	26.4	52	28.6	0.56
39 - < 52	31	32.6	35	40.2	66	36.3	
$\geq$52	35	36.8	29	33.3	64	35.2	
Height(cm)							
< 147	26	27.4	26	29.9	52	28.6	0.16
147 - <157	42	44.2	27	31.0	69	37.9	
$\geq$157	27	28.4	34	39.1	61	33.5	
Total	95	100	87	100	182	100	

* p value for seasonal differences

Table 2: Morning and evening FEV_1 expressed as a percentage of predicted, and diurnal FEV_1change expressed as 100*(FEV_1 bedtime - FEV_1 morning)/ FEV_1 morning among 182 asthmatic children, by season Windsor, 2005.

Variables	Mean (SD)	1st Quartile	Median	3rd Quartile
Percentage of predicted FEV_1				
Morning	83.8 (18.1)	73.5	85.3	95.3
Evening	84.5 (18.3)	74.0	85.8	95.9
Diurnal FEV_1 change(%)	2.28 (17.4)	-5.6	0.4	7.6

Table 3: Frequency distribution of the daily 24-hr mean concentrations of selected outdoor air pollutants and meteorological characteristics in Windsor, between October 11 and December 11, 2005.*

Pollution/weather variable	Days	Mean	Standard deviation	25th percentile	Median	75th percentile	Interquartile range
SO_2 (ppb)	56	6.0	4.8	2.3	4.5	8.8	6.5
NO_2(ppb)	56	19.1	6.0	14.5	19.8	24.3	9.8
O_3 (ppb)	56	14.1	6.0	8.8	13.0	17.8	9.0
O_3 max (ppb)	56	27.2	8.6	21.8	27.0	32.8	11.0
$PM_{2.5}$ ($\mu g/m^3$)	56	7.8	5.0	4.0	6.5	10.0	6.0
Temperature (ºC)*	56	5.3	7.2	-1.9	6.6	11.1	13.0
Relative humidity (%)	56	67.0	8.6	60.2	67.4	71.8	11.6

***** Data were obtained from Environment Canada's National Air Pollution Surveillance (NAPS) network

Table 4: Pearson correlation coefficients (p-values) between daily mean measures of outdoor air pollution, temperature and relativity humidity, Windsor, October 11 to December 11, 2005

Pollutants	NO_2	O_3	O_3max	$PM_{2.5}$	Temperature	Relative humidity
SO_2	0.31 (0.02)	-0.05 (0.70)	-0.02 (0.90)	0.43 (<0.001)	-0.30 (0.03)	-0.19 (0.16)
NO_2	1	-0.50 (<0.001)	-0.18 (0.19)	0.68 (<0.001)	-0.11 (0.40)	0.00 (0.99)
O_3		1	0.81 (<0.0001)	-0.26 (0.05)	0.09 (0.51)	-0.55 (<0.001)
O_3max			1	-0.03 (0.82)	0.28 (0.04)	-0.51 (<0.001)
$PM_{2.5}$				1	0.17 (0.22)	0.14 (0.32)
Temperature					1	0.09 (0.51)

Table 5: The change in bedtime percentage of predicted FEV_1 associated with an interquartile increase in daily air pollutant concentration averaged between 8:00pm the previous day to 8:00pm on the test day, among children with asthma in Windsor, October 11 to December 11, 2005*

Pollutants	Air pollution averaging time (hr)	Change in percentage of predicted FEV_1	95% CI	P-value
NO_2	0 - 12	-0.10	(-0.31, 0.10)	0.32
	12 - 24	-0.09	(-0.41, 0.23)	0.58
	0 - 24	-0.24	(-0.79, 0.30)	0.38
O_3 max	0 - 12	0.31	(-0.36, 0.98)	0.36
	12 - 24	-0.15	(-0.61, 0.32)	0.54
	0 - 24	-0.13	(-0.52, 0.28)	0.54
$PM_{2.5}$	0 - 12	-0.39	(-0.79, 0.01)	0.06
	12 - 24	-0.32	(-0.71, 0.07)	0.11
	0 - 24	-0.54	(-1.02, -0.06)	0.03
SO_2	0 - 12	-0.11	(-0.64, 0.41)	0.67
	12 - 24	0.00	(-0.60, 0.60)	0.99
	0 - 24	-0.09	(-0.67, 0.49)	0.75

* A mixed model was used with random intercept and fixed slope. Associations were adjusted for daily mean temperature, relative humidity, day of week, outdoor activity on the same day of at least 2 hours, and study period (Oct 11 - Nov 7, Nov 14 - Dec 11).

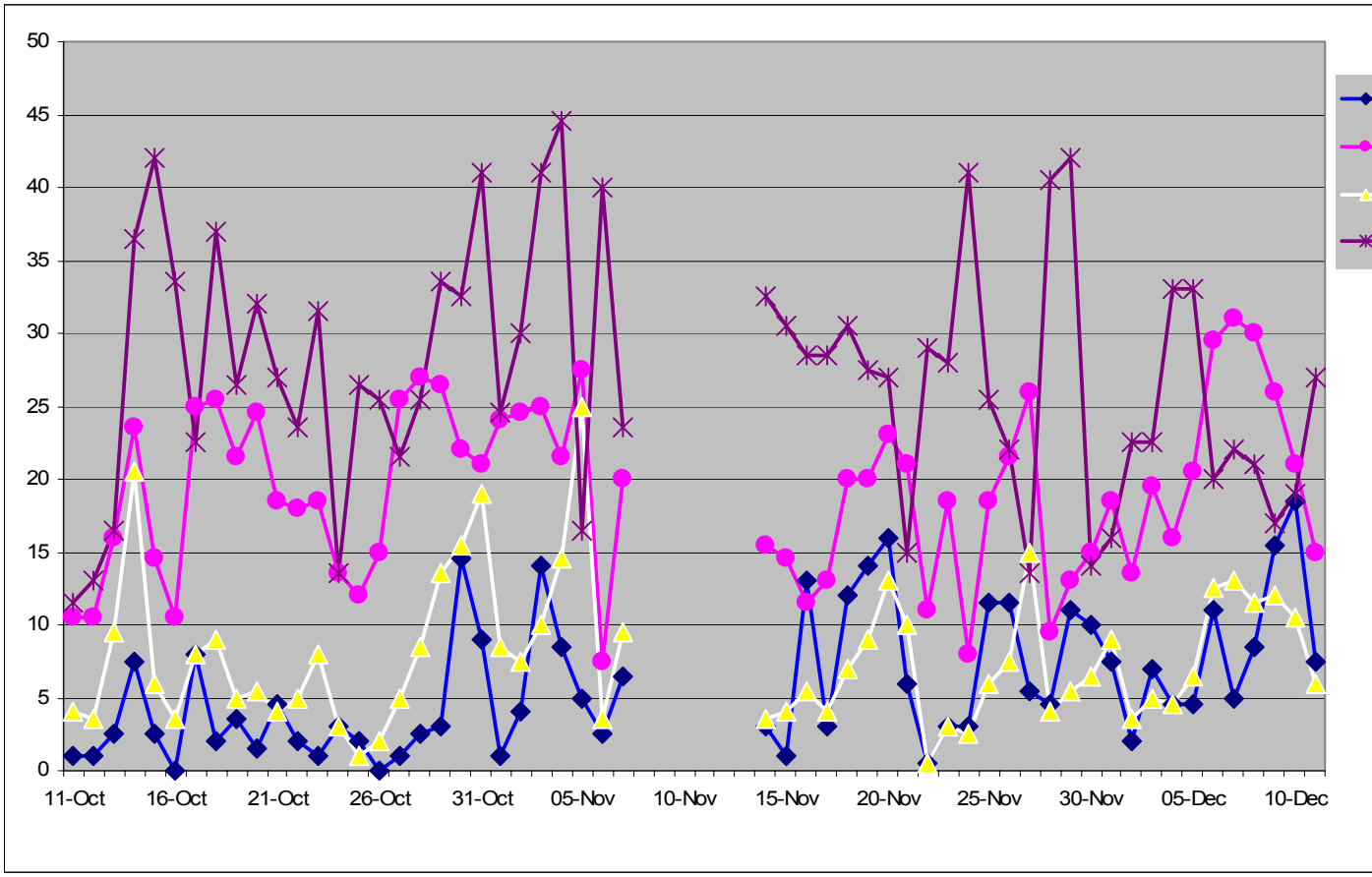
Table 6: The diurnal change in FEV_1 expressed as 100*(FEV_1 bedtime - FEV_1 morning)/ FEV_1 associated with an interquartile increase in the daily air pollutant concentration averaged between 8:00a.m.and 8:00pm on the test day, among children with asthma in Windsor, October 11 to December 11, 2005*

Pollutants	Air pollution averaging time (hr)	Diurnal change in FEV_1	95% CI	P-value
NO_2	0 - 12	-0.34	(-0.64, -0.04)	0.02
O_3max	0 - 12	0.75	(-0.33, 1.83)	0.18
$PM_{2.5}$	0 - 12	-0.73	(-1.37, -0.10)	0.02
SO_2	0 - 12	-0.92	(-1.78, -0.06)	0.04

* A mixed model was used with random intercept and fixed slope. Associations are adjusted for daily mean temperature, relative humidity, day of week, outdoor activity on the same day of at least 2 hours, and study period (Oct 11 - Nov 7, Nov 14 - Dec 11).

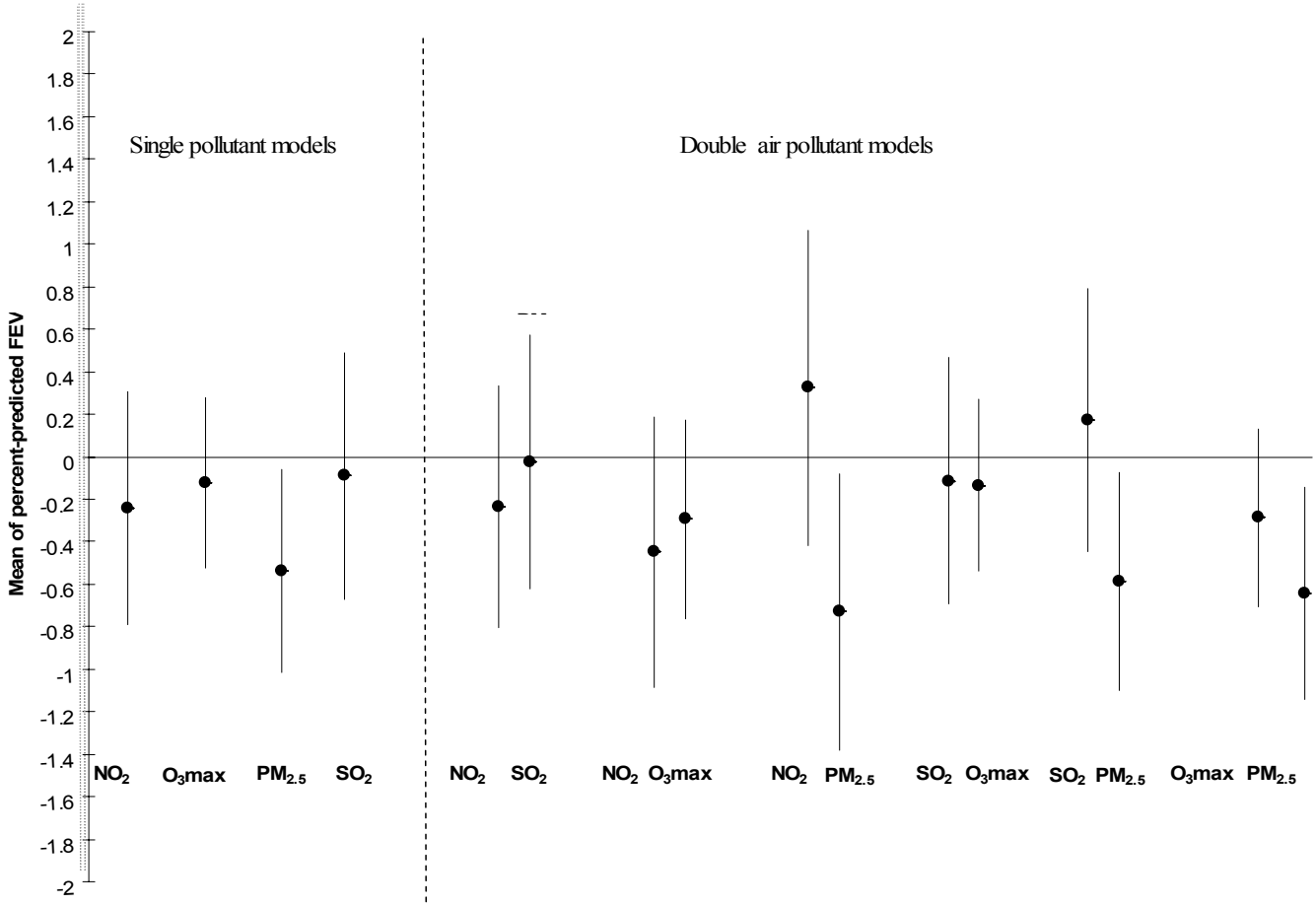
Legend for Figure 1. Twenty-four hour mean concentrations of air pollutants during the study period October 11 to December 11, 2005 in Windsor, Canada. All pollutant concentrations on Y-axis are expressed in ppb except $PM_{2.5}$ which is in $\mu g/m^3$

Figure1.


50
45
40
35
30
25
20
15
10
5
0
11-Oct
16-Oct
21-Oct
26-Oct
31-Oct
05-Nov
10-Nov
15-Nov
20-Nov
25-Nov
30-Nov
05-Dec
10-Dec

Legend for Figure 2 Mean (95% CI) bedtime FEV_1expressed as a percentage of predicted, associated with interquartile increase of air pollutant concentration. We used a mixed model with autoregressive covariance structure adjusted for daily mean temperature, relative humidity, day of week, time for outdoor activity on the same day, study period (Oct 11 - Nov 7, Nov 14 - Dec 11).

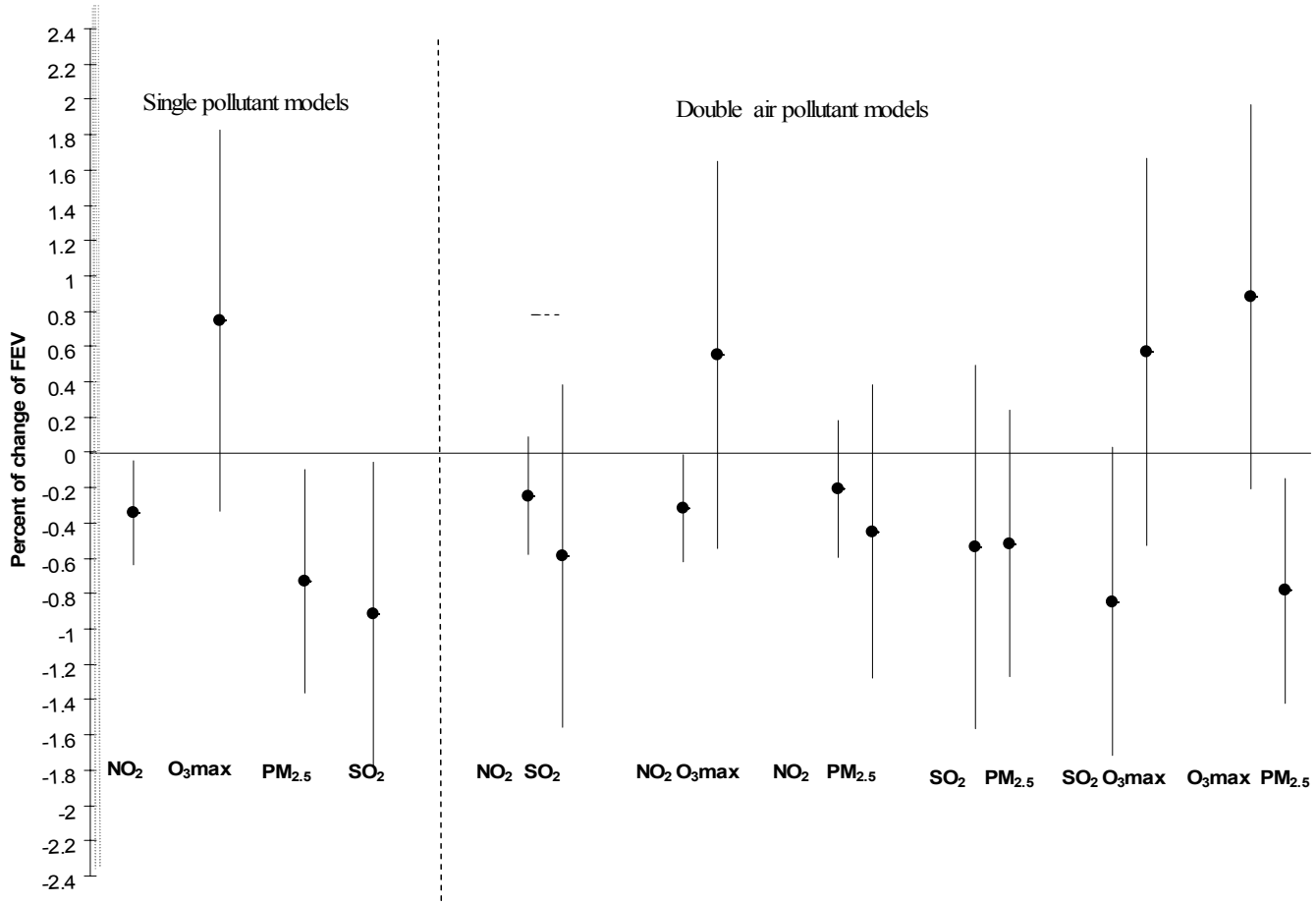
1 Figure 2


Mean of percent-predicted FEV
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1
-1.2
-1.4
-1.6
-1.8
-2
Single pollutant models
Double air pollutant models
NO2
O3max
PM2.5
SO2
NO2
SO2
NO2
O3max
NO2
PM2.5
SO2
O3max
SO2
PM2.5
O3max
PM2.5

2

Legend for Figure 3. Mean (95% CI) for diurnal change in FEV_1 associated with interquartile increases of air pollutant concentrations averaged from 8 am – 8 pm on the test day. We used a mixed model with autoregressive covariance structure adjusted for daily mean temperature, relative humidity, day of week, time for outdoor activity on the same day, study period (Oct 11 - Nov 7, Nov 14 - Dec 11).

Figure 3.


Single pollutant models
Double air pollutant models
Percent of change of FEV
2.4
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1
-1.2
-1.4
-1.6
-1.8
-2
-2.2
-2.4
NO2
O3max
PM2.5
SO2
NO2 SO2
NO2 O3max
NO2 PM2.5
SO2 PM2.5
SO2 O3max
O3max PM2.5