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ORIGINAL ARTICLE Short-term risk of hospitalization for asthma or bronchiolitis in children living near an aluminum smelter

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Few studies have measured the effect of short-term exposure to industrial emissions on the respiratory health of children. Here we estimate the risk of hospitalization for asthma and bronchiolitis in young children associated with their recent exposure to emissions from an aluminum smelter. We used a case–crossover design to assess the risk of hospitalization, February 1999– December 2008, in relation to short-term variation in levels of exposure among children 0–4 years old living less than 7.5 km from the smelter. The percentage of hours per day that the residence of a hospitalized child was in the shadow of winds crossing the smelter was used to estimate the effect of wind-borne emissions on case and crossover days. Community-wide pollutant exposure was estimated through daily mean and daily maximum SO₂ and PM_{2.5} concentrations measured at a fixed monitoring site near the smelter. Odds ratios (OR) were estimated using conditional logistic regressions. The risk of same-day hospitalization for asthma or bronchiolitis increased with the percentage of hours in a day that a child's residence was downwind of the smelter. For children aged 2–4 years, the OR was 1.27 (95% CI = 1.03-1.56; n = 103 hospitalizations), for an interquartile range (IQR) of 21% of hours being downwind. In this age group, the OR with PM_{2.5} daily mean levels was slightly smaller than with the hours downwind (OR: 1.22 for an IQR of $15.7 \mu g/m^3$, 95% CI = 1.03-1.44; n = 94 hospitalizations). Trends were observed between hospitalizations and levels of SO₂ for children 2–4 years old. Increasing short-term exposure to emissions from a Quebec aluminum smelter was associated with an increased risk of hospitalization for asthma and bronchiolitis in young children who live nearby. Estimating exposure through records of wind direction allows for the integration of exposure to all pollutants carried from the smelter stack.

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INTRODUCTION

Epidemiological studies suggest that short-term exposure to ambient air pollution is related to adverse consequences on children's respiratory health.¹ Acute as well as chronic respiratory effects have been noted for exposure to sulfur dioxide (SO₂) and fine particles ($PM_{2,5}$).

Most epidemiological studies that assess the respiratory effects of industrial emissions in children use a cross-sectional design. These studies typically report lower lung functions or a higher prevalence of asthma or respiratory symptoms in children living in proximity to important air pollutant emitters such as cement smelters, steel mills, foundries and refineries.^{2–13} Increased bronchial hyper-responsiveness has also been reported.^{14–16} Cross-sectional designs do however, make it difficult to separate the effects of one or many high-level past exposures from ongoing lower-level exposure; further, in cross-sectional studies, out-migration of affected individuals reduces estimates of the effect of exposure.

The acute respiratory effects of children's exposure to ambient SO_2 or $PM_{2.5}$ have been studied in panel studies and in population-based time series analyses. These studies have been performed primarily in urban areas, with the aim of assessing

population responses to ambient air pollutants, rather than to emissions from specific industries. Typically, they report associations between daily variations in urban ambient SO_2 and $PM_{2.5}$ levels and a variety of acute respiratory effects including airway hyper-responsiveness, respiratory symptoms, emergency department visits and hospital admissions for respiratory causes, in particular, asthma.^{17,18}

To date, few studies have assessed the acute respiratory effects in children of exposure to industrial SO₂ and PM_{2.5} air emissions. In a recent study, Smargiassi et al.¹⁹ used a case–crossover design to assess the acute respiratory effects on young children, of SO₂ emitted from nearby petroleum refineries. An increased risk of emergency room visits and hospitalizations for asthma, as a function of daily variation in SO₂ levels, was found for children 2–4 years of age.

The aim of the present study was to compare estimates of the risk of hospitalization for asthma and bronchiolitis in children under 5 years of age in relation to their recent exposure to emissions from an aluminum smelter in Shawinigan, Quebec (Canada) as a function of SO_2 and $PM_{2.5}$ measured at a single fixed monitoring station versus exposure to winds blowing over the smelter and toward their homes.



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METHODS

Study Area, Period and Population

According to the Environment Canada's National Pollutant Release Inventory (NPRI), in 2008 the Shawinigan aluminum smelter was the second-most important industrial emitter of $PM_{2.5}$ in the Province of Quebec, with 1034 tons emitted and ranked 20th for discharges of SO_2 (2192 tons). The smelter was also the most important industrial benzo(a)pyrene (BaP) emitter in Quebec, with 65% of Quebec's (7705 kg in 2008) emissions overall.²⁰

Surrounded by residential neighborhoods, in 2002, the aluminum smelter became the sole heavy industrial emitter in Shawinigan (Figure 1). A silicon carbide production plant located in the study area was also an important $PM_{2.5}$ emitter before it closed in 2001.

The study area was defined by a 7.5-km buffer around the aluminum smelter. This captured almost the entire population of Shawinigan; in 2006, there were 910 children aged between 0 and 4 years living in the study area.²¹



Hospitalizations were identified through the calendar period 1 February 1999 to 31 December 2008. These occurred in children aged 0 and 4 years who lived in the study area and who were hospitalized for asthma or bronchiolitis (as primary cause). The latter was retained, as the diagnosis of asthma among children younger than 2 years old is problematic and often confused with bronchiolitis.²² The study was restricted to children under 5 years old, as they are likely more susceptible to air pollution-related health effects than older children.²³ Case–crossover analyses have also shown a greater excess of asthma hospitalizations associated with petroleum refinery emissions for children of 2–4 years of age than for other age groups.¹⁹

Health Data

Hospitalization data were extracted from the MED–ECHO database of the Quebec Ministry of Health and Social Services. MED–ECHO captures virtually all hospitalizations in Quebec residents.²⁴ Data extracted included the following individual-level information: time

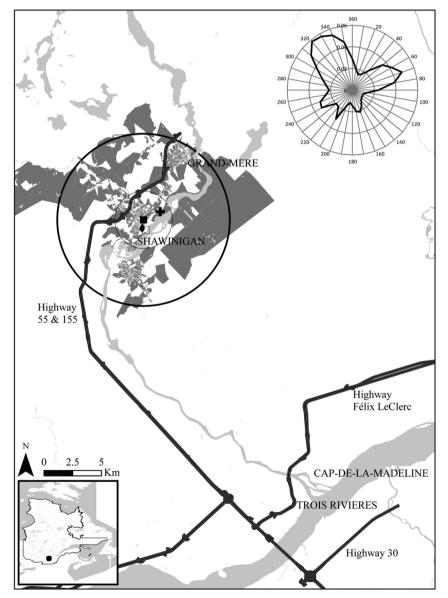


Figure 1. Residential study area within the 7.5-km buffer around the aluminum smelter and subpopulation located within the 2.5-km buffer around the industry. The wind rose for the hourly wind data for the study period (1999–2008) is also presented. The cross represents the meteorological station, the square is the smelter and the diamond represents the pollutant-monitoring station.

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and date of the hospitalization, the primary cause of hospitalization, and patient characteristics such as age, sex, and the six-character postal code of the hospitalized child's place of residence. Hospitalizations for asthma were identified in MED-ECHO by the ICD-9 and ICD-10 codes 493 and J45-J46 and hospitalizations for bronchiolitis, by the ICD-9 and ICD-10 codes 466 and J21 (*International Classification of Diseases, 9th and 10th Revisions,* ICD-9 and ICD-10).

Exposure to Industrial Emissions

Exposure to smelter emissions was estimated by 1) the percentage of hours per day that the hospitalized child's residence was downwind of the smelter; 2) SO_2 and $PM_{2.5}$ concentrations measured at a single fixed-site monitoring station.

The percentage of hours per day that the hospitalized child's residence was downwind of the smelter was determined using the geographic centroid of the full six-character postal code at their residence and hourly wind directions and speed recorded at a meteorological station located at 1.6 km North-East of the smelter. We acquired meteorological data from Environment Canada:²⁵ using 36 wind directions, all postal codes located within an opening angle of 45°, that is, within 22.5° of either side of the wind vector originating at the smelter stack, were considered exposed to the smelter's emissions. When there was no wind (1.4% of the time), all residences located within 2.5 km of the smelter were considered exposed. The percentage of downwind hours per day was estimated using the number of hours that the residence was downwind divided by the number of recorded wind hours available. Days with less than 18 h of wind direction records were considered as missing. Wind directions for the study period overall are presented in the wind rose in Figure 1.

Ambient concentrations of SO_2 and $PM_{2.5}$ were measured by Environment Canada²⁶ at their National Air Pollution Surveillance Program (NAPS) monitor located 600 m south of the aluminum smelter (Figure 1). Both daily mean and daily hourly maximum were considered.

Statistical Analyses

Associations between exposure variables and hospitalizations were studied using a case–crossover design. Control days were selected using a time-stratified approach,²⁷ in which we divided the study period into monthly strata and selected control days for each case as the same days of the week during the month. Thus, if a hospitalization occurred on Tuesday, 24 May 2005 (corresponding to the hazard period, lag 0), the selected control periods were on Tuesdays of the same month (3, 12, 17, and 31 May 2005). By doing so, we removed biases from unwanted secular trends in the hospitalization time series.^{28,29}

Associations between hospitalizations and the exposure variables (i.e., percentage of downwind hours per day; daily means and hourly peaks of SO_2 and $PM_{2.5}$) were assessed by conditional logistic regression analyses using the R statistical software (http://www.R-project.org). The linearity of the relations between hospitalizations and the exposure variables was verified visually.

Analyses were conducted for the entire study population (children 0–4 years old living within 7.5 km from the smelter) and for a sub-group whose residences were within 2.5 km from the smelter (Figure 1). All exposure variables were assessed separately. Strata with fewer than 3 control days were excluded.

Odd ratios (ORs) and their 95% confidence intervals (95% CIs) were expressed over an interquartile range (IQR) defined as the difference between the first (Q1) and the third (Q3) quartile of the exposure variable. Analyses are presented for the age group 0–4 years. Sub-analyses for the 0–1 and the 2–4 age groups were also performed.

Sensitivity analyses were performed for hospitalizations that occurred after the closure of the silicon carbide production plant

in 2001. Sensitivity analyses were also performed excluding repeat hospitalizations within a window of 30 days to reduce overlap in time of exposures/hospitalization. Secondary analyses were also performed, controlling for average daily wind speed. Furthermore, analyses were performed using exposure on days before the case or the control dates (lag1, average of lag0 and lag1 and average of lag0 to lag2), in addition to the concurrent exposure day (lag0). Finally, analyses with air pollutants were performed with a 2.5-km buffer around the air pollution monitoring station in addition to the 2.5-km buffer around the smelter.

RESULTS

Table 1 shows the percentage of daily hours that the study population was downwind of the aluminum smelter, as well as $PM_{2.5}$ and SO_2 concentrations measured at the monitoring station. Maximum daily $PM_{2.5}$ and SO_2 concentrations reached high levels (967 μ g/m³ and 434 p.p.b., respectively). Based on wind data, we estimated that the study population was, on an average located downwind of the smelter 14.6% ± 4.9% of hours per day.

A total of 429 hospitalizations of children aged from 0 to 4 years for asthma or bronchiolitis occurred in the study area: of these, 321 were of children aged 0-1 years (99 for asthma) and 108 (101 for asthma) were of children 2-4 years of age. Of the 429 hospitalizations, 47 were excluded from analyses of the association between respiratory hospitalizations and wind exposure due to missing wind data (case or control dates) in case-crossover strata. Of the 396 hospitalizations remaining, 109 were included in the sub-group living within 2.5 km of the smelter. Table 2 presents associations between hospitalizations for asthma or bronchiolitis and the percentage of hours that the children's residences were downwind of the smelter stack. Similar results were found comparing the entire study population and the sub-group living within 2.5 km of the smelter. ORs obtained for both sub-age groups were greater or equal to 1, with greater associations found for the 2- to 4-year group. Statistical significance was only reached for the latter (OR: 1.27 with an IQR of 21% of hours being downwind; 95% CI: 1.03-1.56).

Table 3 shows associations between hospitalizations for asthma or bronchiolitis and ambient levels of SO_2 and $PM_{2.5}$ (daily mean and hourly maximum). Among hospitalizations of children living within 7.5 km of the smelter, 400 and 365 were matched to SO_2

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Exposure variable	n	Mean ± SD	Min–max
Exposure to the wind from the smelter (% of hours per day)	10,277,720 ^a	14.6% ± 4.9% ^b	0%-100%
PM _{2.5} (μg/m ³) Daily mean Hourly max	3391 ^c	13.5 ± 16.0 50.0 ± 73.9	0.08–335.0 2.0–967.0
SO ₂ (p.p.b.) Daily mean Hourly max	3580 ^d	6.3 ± 10.1 24.5 ± 41.4	0–168.0 0–434.0

^aNumber of receptor points (2887 six-character residential postal codes in the study area) \times 3560 days of wind data. 62 days were missing wind data. ^bPopulation-weighted daily mean exposure of all postal codes located in the study area.

^c231 days were missing PM_{2.5} data.

^d42 days were missing SO_2 data.

and $PM_{2.5}$ data respectively, whereas for the subpopulation living within 2.5 km of the smelter, 112 hospitalizations were matched to SO_2 data and 101 to $PM_{2.5}$. ORs found for the 7.5-km buffer around the aluminum smelter were similar to those obtained for the 2.5-km buffer; ORs calculated using the daily mean were greater than those calculated with the daily maximum. While ORs were close or less than 1 for the 0- to 1-year group, ORs for the 2- to 4-year group was greater than 1 but did not reach statistical significance except for $PM_{2.5}$. Associations with $PM_{2.5}$ levels were slightly smaller than those observed estimating exposure as the percentage of hours downwind.

 Table 2.
 Hospitalizations for asthma or bronchiolitis in children aged

 0-4 years versus percentage of hours per day that their residence was downwind of the aluminum smelter.

Age group (years)	N Total (n hospitalisations)	IQR (h/day)	OR (95% CI)
	7.5 km buffer around th	ne aluminum sm	nelter
0–4 ^a	1740 (396)	25% (6)	1.08 (0.95-1.23
0–1	1290 (293)	29% (7)	1.00 (0.84-1.20
2–4	450 (103)	21% (5)	1.27 (1.03–1.56
	2.5 km buffer around th	ne aluminum sm	nelter
0–4 ^b	478 (109)	25% (6)	1.22 (0.93-1.61
0–1	354 (81)	27% (6.5)	1.08 (0.76-1.53
2–4	124 (28)	17% (4)	1.45 (1.00-2.12

missing meteorological data in case-crossover strata. ^b10 cases (i.e., 10 case days + 40 controls days) were excluded due to missing meteorological data in case-crossover strata. Sensitivity analyses showed that results were essentially the same when only hospitalizations, which occurred after the closure of the second factory in 2001 were considered. Results were also virtually the same when restricting analyses with air pollutants to children living within 2.5 km of the monitoring station instead of within 2.5 km of the smelter. Furthermore, wind speed did not influence the associations with the exposure variables (data not shown). As for associations using exposure on lag 1 and the average of exposure on lag 0 and lag 1, stronger odds ratios were also observed for hours downwind than for pollutants (Appendix Tables A1 and A2). Finally, analyses performed excluding repeat hospitalizations within 30 days (\sim 5% of hospitalizations) provided similar results (Appendix Tables A1 and A2).

DISCUSSION

This study showed associations between hospitalizations for asthma or bronchiolitis in young children (0–4 years) and recent residential exposure to the emissions of a nearby aluminum smelter. Unlike most epidemiological studies that have investigated the acute effects of exposure to daily ambient regional air pollutant concentrations, our study was not performed in an urban area but in a small industrial town. The contribution of other sources of air pollutants was negligible: the only other large emitter of PM_{2.5} in the area closed in 2001, during the first third of the study period. Sensitivity analyses showed similar effects including, and excluding hospitalizations that occurred when the second regional emitter was in operation.

Overall, ORs obtained for the population living in a buffer of 7.5 km around the aluminum smelter were quite similar to those obtained for the population living within 2.5 km of the smelter. We found a modest association between hospitalizations for asthma or bronchiolitis in children 0–4 years old

Age group (years)	n Total (n hospitalizations)	Daily mean		Hourly max	
		IQR	OR (95% CI)	IQR	OR (95% CI)
	7.5 km bu	Iffer around the all	ıminum smelter		
SO ₂ (p.p.b.)					
0–4 ^a	1762 (400)	9.35	1.02 (0.95–1.10)	48.00	1.03 (0.93–1.16
0–1	1300 (295)	9.70	0.98 (0.89-1.08)	48.00	1.02 (0.90–1.15
2–4	462 (105)	8.44	1.11 (0.97–1.25)	45.75	1.11 (0.89–1.38
РМ _{2.5} (µg/m³)					
0-4 ^b	1604 (365)	15.04	1.03 (0.94–1.12)	57.00	1.01 (0.94–1.10
0–1	1191 (271)	14.26	0.96 (0.86–1.07)	57.00	0.97 (0.89–1.07
2–4	413 (94)	15.70	1.22 (1.03–1.44)	57.50	1.16 (0.99–1.36
	2.5 km bi	Iffer around the all	ıminum smelter		
SO ₂ (p.p.b.)					
0–4 ^c	490 (112)	10.37	1.02 (0.89–1.18)	48.00	0.98 (0.80–1.20
0–1	366 (84)	10.35	0.93 (0.76–1.15)	47.00	0.95 (0.75–1.19
2–4	124 (28)	9.34	1.14 (0.95–1.37)	51.25	1.10 (0.72–1.71
PM _{2.5} (μg/m ³)					
$0-4^{d}$	440 (101)	17.37	1.04 (0.86–1.26)	60.50	1.01 (0.87–1.17
0-1	329 (76)	16.25	0.93 (0.73–1.19)	62.00	0.98 (0.82–1.18
2–4	111 (25)	18.08	1.21 (0.91–1.61)	56.75	1.07 (0.85–1.34

²29 cases (i.e., 29 case days + 106 controls days) were excluded due to missing meteorological data in case-crossover strata.

^b64 cases (i.e., 64 case days + 276 controls days) were excluded due to missing meteorological data in case-crossover strata.

^c10 cases (i.e., 10 case days + 41 control days) were excluded from analysis due to missing SO₂ data in strata ^d22 cases (i.e., 23 case days + 95 control days) were excluded from analysis due to missing PM_{2.5} data in strata.

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and the percentage of hours per day that their residences were subject to winds blowing over the smelter as well as with $PM_{2.5}$ levels. We observed greater ORs for the 2- to 4-year age group than for the 0- to 1-year- and 0- to 4-year-olds. This may be in part due to less imprecision in the diagnosis of wheezy respiratory disease for children aged 2–4 years than for younger children.

Smaller associations were found between hospitalization and SO_2 and $PM_{2.5}$ concentrations than with wind data. That residential downwind estimates allow all emitted air pollutants to be considered together might explain the more pronounced association observed for wind data as compared with pollutant concentrations. Perhaps more relevant is that industrial air-quality monitors are placed to capture pollutants arising from major emitters, and are not necessarily situated to best assess population exposure. In any case, monitored pollutant concentrations living with the smelter between them and the monitor.

On a population level, the association found between hours downwind and hospitalizations in young children translates into modest impacts on overall health. Indeed, based on the association obtained between hospitalizations and wind data (OR = 1.27 per an IQR of 21% of the time downwind; 95% CI = 1.03–1.56), the number of cases observed during the study period and the hours overall that children's residences would have been downwind of the smelter, we estimate an attributable number (AN) of hospitalizations for asthma or bronchiolitis in 2- to 4-year-old children due to exposure to smelter emissions of ~ 2 per year (AN = 1.8; 95% CI = 0.3–3.0). Nonetheless, many more children living in proximity to the smelter may experience symptoms not leading to hospitalization.

Our results are difficult to compare with previous findings, as time spent downwind has not commonly been used to represent exposure to industrial emissions for the assessment of acute respiratory effects. Wind data have however been used by others to assess risks associated with exposure to industrial emissions. White et al.,³⁰ in a cross-sectional study, developed an individual meteorological exposure indicator, based on a velocity-weighted average of wind exposure, and using residential distance of each child from a refinery, with 16 compass wind direction segments. They found a positive association between their indicator and the prevalence of respiratory symptoms in children aged 11–14 years old (e.g., OR for recent waking with wheezing: 1.33, 95% CI: 1.06–1.66 per IQR).

Few studies have assessed the risk of childhood asthma episodes associated with SO₂ and PM_{2.5} from a point source. Our results for SO₂ can be compared with Smargiassi et al.,¹⁹ who also used a case–crossover design to assess the risk of asthmatic episode in children exposed to SO₂ stack emissions from a refinery point source. Smargiassi et al.¹⁹ reported an OR of 1.14 (95% CI: 1.02–1.29) for hospitalizations in children 2–4 years of age for an IQR of 6.3 p.p.b. in daily mean SO₂ concentrations. This is concordant with our findings for 2- to 4-year-olds (living at <7.5 km from the smelter) of an OR of 1.11 for an IQR of 8.44 p.p.b. in daily mean SO₂. However, Smargiassi et al.¹⁹ observed a more pronounced risk of hospitalizations for asthma for peaks of SO₂ than for daily means, which was not the case in the current study.¹⁹

As with many epidemiological studies that investigate the adverse health effects of ambient air pollutants, a limitation is the estimation of individual exposure, in our case using children's residential location as a surrogate. Even if children are more likely to stay in their neighborhood than adults, they may not be at home all day. In addition, ambient concentrations might overestimate children's exposure, as they spend more time indoors, where pollutant concentrations are known to be lower than outdoors.³¹ Nonetheless, the percentage of hours spent downwind appears to be a relevant and simple exposure metric

to estimate acute community health risks associated with industrial emissions. It can allow for the assessment of exposure to mixtures of pollutants from a single emitter, as mixtures may have additive, synergistic or antagonistic effects. It is compatible with a case–crossover design allowing for smaller sample sizes.

CONCLUSION

The current study is the first to assess the acute risk of hospitalization for asthma and bronchiolitis in young children exposed to emissions from an aluminum smelter. Our results suggest that increasing daily exposure to emissions from an aluminum smelter, as reflected by hours resident downwind, is associated with an increased risk of hospitalization in young children who live nearby. Estimating exposure based on wind direction allows all pollutants carried from the smelter stack to be captured and overcomes the limitations of monitoring stations, which are often too few, or not optimally situated, to assess acute risks associated with exposure to point source emitters.

ABBREVIATIONS

AN, attributable number; BaP, Benzo(a)pyrene; 95% CI, 95% confidence intervals; ICD, International Classification of Diseases; IQR, interquartile range; NAPS, National Air Pollution Surveillance; NPRI, National Pollution Release Inventory; OR, odd ratio; PM_{2.5}, fine particles; particles with median diameter of 2.5 μ m; Q1, first quartile; Q3, third quartile; SO₂, sulfur dioxide

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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ETHICS

The project was carried out in the context of the Quebec ministerial health surveillance plan, which obtained ethics approval from the Quebec Public Health Ethical Health Surveillance Committee.

REFERENCES

- 1 WHO. Air quality and health. world health organisation, Fact sheet, N°313. 2011; Available from http://www.who.int/mediacentre/factsheets/fs313/en/index.html.
- 2 Brabin B, Smith M, Milligan P, Benjamin C, Dunne E, Pearson M. Respiratory morbidity in Merseyside schoolchildren exposed to coal dust and air pollution. *Arch Dis Child* 1994; **70**: 305–312.
- 3 Dales RE, Spitzer WO, Suissa S, Schechter MT, Tousignant P, Steinmetz N. Respiratory health of a population living downwind from natural gas refineries. *Am Rev Respir Dis* 1989; **139**: 595–600.
- 4 de Marco R, Marcon A, Rava M, Cazzoletti L, Pironi V, Silocchi C *et al.* Proximity to chipboard industries increases the risk of respiratory and irritation symptoms in children: the Viadana study. *Sci Total Environ* 2010; **408**: 511–517.
- 5 Ginns SE, Gatrell AC. Respiratory health effects of industrial air pollution: a study in east Lancashire, UK. *J Epidemiol Community Health* 1996; **50**: 631–635.
- 6 Goren A, Hellmann S, Gabbay Y, Brenner S. Respiratory problems associated with exposure to airborne particles in the community. Arch Environ Health 1999; 54: 165–171.
- 7 Heinrich J, Hoelscher B, Wjst M, Ritz B, Cyrys J, Wichmann H. Respiratory diseases and allergies in two polluted areas in East Germany. *Environ Health Perspect* 1999; 107: 53–62.
- 8 Hurry VM, Peat JK, Woolcock AJ. Prevalence of respiratory symptoms, bronchial hyperresponsiveness and atopy in schoolchildren living in the Villawood area of Sydney. Aust NZ J Med 1988; 18: 745–752.
- 9 Kobrossi R, Nuwayhid I, Sibai AM, El-Fadel M, Khogali M. Respiratory health effects of industrial air pollution on children in North Lebanon. *Int J Environ Health Res* 2002; **12**: 205–220.

- 10 Lewis PR, Hensley MJ, Wlodarczyk J, Toneguzzi RC, Westley-Wise VJ, Dunn T et al. Outdoor air pollution and children's respiratory symptoms in the steel cities of New South Wales. *Med J Aust* 1998; **169**: 459–463.
- 11 Nystad W, Magnus P, Roksund O, Svidal B, Hetlevik O. The prevalence of respiratory symptoms and asthma among school children in three different areas of Norway. *Pediatr Allergy Immunol* 1997; **8**: 35–40.
- 12 Spektor DM, Hofmeister VA, Artaxo P, Brague JA, Echelar F, Nogueira DP *et al.* Effects of heavy industrial pollution on respiratory function in the children of Cubatao, Brazil: a preliminary report. *Environ Health Perspect* 1991; **94**: 51–54.
- 13 Wichmann FA, Muller A, Busi LE, Cianni N, Massolo L, Schlink U *et al.* Increased asthma and respiratory symptoms in children exposed to petrochemical pollution. *J Allergy Clin Immunol* 2009; **123**: 632–638.
- 14 Forastiere F, Corbo GM, Pistelli R, Michelozzi P, Agabiti N, Brancato G *et al.* Bronchial responsiveness in children living in areas with different air pollution levels. *Arch Environ Health* 1994; **49**: 111–118.
- 15 Henry RL, Abramson R, Adler JA, Wlodarcyzk J, Hensley MJ. Asthma in the vicinity of power stations: I. A prevalence study. *Pediatr Pulmonol* 1991; 11: 127–133.
- 16 Soyseth V, Kongerud J, Haarr D, Strand O, Bolle R, Boe J. Relation of exposure to airway irritants in infancy to prevalence of bronchial hyper-responsiveness in schoolchildren. *Lancet* 1995; **345**: 217–220.
- 17 US-EPA. Integrated Science Assessment for Sulfur Oxides Health Criteria (Final Report). US Environmental Protection Agency: Washington, DC 2008, Contract No.: EPA/600/R-08/047F.
- 18 US-EPA. Integrated Science Assessment for Particulate Matter (Final Report). US Environmental Protection Agency: Washington, DC 2009, Contract No.: EPA/600/ R-08/139F.
- 19 Smargiassi A, Kosatsky T, Hicks J, Plante C, Armstrong B, Villeneuve PJ et al. Risk of asthmatic episodes in children exposed to sulfur dioxide stack emissions from a refinery point source in Montreal, Canada. Environ Health Perspect 2009; 117: 653–659.
- 20 Environment-Canada. National Pollutant Release Inventory (NPRI). 2008 (updated November 6 2012) Available from: http://www.ec.gc.ca/pdb/websol/querysite/ facility_substance_summary_e.cfm?opt_npri_id=0000003057&opt_report_year=2008.

APPENDIX

Table A1. Associations between hospitalizations for asthma or bronchiolitis in children aged 0–4 years *versus* percentage of hours per day that their residence was found downwind from the aluminum smelter (A) lagged for lag 1 day; (B) for the average of lags 0 and 1 day; (C) excluding repeat hospitalizations of kids that occurred within 30 days.

Age group (years)	N Total (n hospitalizations)	IQR (h/j)	OR (95% CI)		
	(A)				
7.5 k	m buffer around the	aluminum sme	lter		
0–4 ^a	1727 (393)	28% (6.7)	1.08 (0.94-1.26)		
0-<2	1285 (292)	28% (6.8)	1.02 (0.86–1.22)		
2–4	442 (101)	25% (6.0)	1.25 (0.98–1.61)		
2.5 k	m buffer around the	aluminum sme	elter		
0–4 ^b	531 (121)	21% (5.0)	1.05 (0.82-1.35)		
0-<2	381 (87)	17% (4.0)	0.99 (0.79-1.25)		
2–4	150 (34)	21% (5.0)	1.27 (0.76–2.1)		
	(B)				
7.5 km buffer around the aluminum smelter					
0–4 ^a	1754 (399)	23% (5.5)	1.11 (0.96-1.29)		
0-<2	1299 (295)	25% (6.0)	, ,		
2–4	455 (104)	22% (5.2)	1.40 (1.08–1.82)		
2.5 k	m buffer around the	aluminum sme	elter		
0–4 ^b	531 (121)	17% (4.0)	1.15 (0.91–1.45)		
0-<2	381 (87)	19% (4.5)	1.04 (0.76-1.42)		
2–4	150 (34)	19% (4.5)	1.57 (0.96-2.57)		

- 21 Statistique-Canada. Census Homepage 2006 Available from http://www12. statcan.gc.ca/census-recensement/index-eng.cfm.
- 22 Panettieri Jr. RA, Covar R, Grant E, Hillyer EV, Bacharier L. Natural history of asthma: persistence *versus* progression-does the beginning predict the end? J Allergy Clin Immunol 2008; **121**: 607–613.
- 23 Bateson TF, Schwartz J. Children's response to air pollutants. J Toxicol Environ Health A. 2008; **71**: 238–243.
- 24 Labreche F, Kosatsky T, Przybysz R. Childhood asthma surveillance using administrative data: consistency between medical billing and hospital discharge diagnoses. *Can Respir J* 2008; **15**: 188–192.
- 25 Environment-Canada. National Climate Data and Information Archive 2011, Available from http://climate.weatheroffice.gc.ca/climateData/menu_e.html?Prov=QC&StationID =99998.Year=2011&Month=9&Day=29&timeframe=1.
- 26 Environment-Canada. National Air Pollution Survey 2011, Available from http:// www.etc-cte.ec.gc.ca/napsdata/Default.aspx.
- 27 Lumley T, Levy D. Bias in the case crossover design: implications for studies of air pollution. *Environmetrics* 2000; **11**: 689–704.
- 28 Janes H, Sheppard L, Lumley T. Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. *Epidemiology* 2005; **16**: 717–726.
- 29 Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. *Am J Epidemiol* 1991; **133**: 144–153.
- 30 White N, teWaterNaude J, van der Walt A, Ravenscroft G, Roberts W, Ehrlich R. Meteorologically estimated exposure but not distance predicts asthma symptoms in schoolchildren in the environs of a petrochemical refinery: a cross-sectional study. *Environ Health* 2009; **8**: 45.
- 31 WHO. Air Quality Guidlines for Europe, 2nd edn. (WHO Regional Publishers: Geneva, 2000.

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(C)					
	7.5 km buffer arou	ind the aluminum si	melter		
0–4 ^a	1631 (372)	25% (6.0)	1.09 (0.95–1.24)		
0-<2	1200 (273)	29% (7.0)	0.99 (0.82-1.20)		
2–4	431 (99)	21% (5.0)	1.29 (1.05–1.59)		

^a36 cases (i.e., 36 case days + 153 control days) were excluded due to missing meteorological data in case-crossover strata. ^b9 cases (i.e., 9 case days + 36 controls days) were excluded due to missing meteorological data in case-crossover strata.

Table A2. Associations between hospitalizations for asthma or bronchiolitis in children 0–4 years of age living nearby the aluminum smelter and daily ambient air pollutant levels: (A) at lag 1 day; (B) mean of lags 0 and 1 day; (C) excluding repeat hospitalizations of kids that occurred within 30 days.

Pollutant age group (years)	N total (n hospitalizations)	Daily mean		ŀ	lourly max
		IQR	OR (95% CI)	IQR	OR (95% CI)
			(A)		
	7.5 km buffe	er around	the aluminum sn	nelter	
SO ₂ (p.p.b.)					
0–4 ^a	1769 (402)	9.83	1.04 (0.96-1.13)	49.00	1.02 (0.91-1.14)
0-<2	1311 (298)	10.04	1.04 (0.94-1.14)	50.00	0.98 (0.86-1.13)
2–4	458 (104)	8.33	1.05 (0.92–1.19)	47.75	1.11 (0.91–1.35)
PM _{2.5} (μg/m ³	3)				
0-4 ⁶	1598 (364)	14.96	1.06 (0.99-1.14)	61.00	1.04 (0.97-1.12)
0-<2	1180 (269)	14.60	1.07 (0.99-1.16)	60.25	1.06 (0.97-1.15)
2–4	418 (95)	15.42	1.03 (0.89–1.20)	60.00	1.01 (0.89–1.15)

2.5 km buffer around the aluminum smelter						
SO ₂ (p.p.b.) 0-4 ^c 0-<2	538 (123) 388 (89)	10.22 10.58	1.06 (0.92–1.21) 1.05 (0.87–1.27)	53.00 53.25	1.03 (0.84–1.26) 1.01 (0.79–1.3)	
2–4	150 (34)	8.55	1.05 (0.88–1.26)	51.75	1.07 (0.75–1.54)	
PM _{2.5} (μg/m	1 ³)					
0-4 ^d 0-<2	488 (112) 351 (81)	15.04 14.87	1.03 (0.91–1.17) 1.02 (0.89–1.17)	54.50 56.00	0.99 (0.88–1.11) 0.98 (0.85–1.13)	
2-4	137 (31)	15.25	1.06 (0.8–1.41)	48.00	1.00 (0.83–1.12)	
	/		(B)			
SO ₂ (p.p.b.)	7.5 ki	n buffer a	round the aluminum	smelter		
0-4 ^e	1815 (413)	9.98	1.04 (0.95–1.15)	45.88	1.03 (0.91-1.18)	
0-<2	1349 (307)	10.04	1.00 (0.89–1.13)	46.63	0.99 (0.85–1.16)	
2–4	466 (106)	9.64	1.14 (0.96–1.35)	42.38	1.14 (0.91–1.42)	
PM _{2.5} (μg/m	n ³)					
0-4 ^r	1688 (380)	15.04	1.07 (0.98–1.18)	54.00	1.04 (0.96–1.14)	
0-<2 2-4	1241 (283) 427 (97)	14.22 16.13	1.04 (0.94–1.15) 1.22 (0.99–1.52)	52.62 56.00	1.02 (0.92–1.12) 1.12 (0.95–1.32)	
2-4	427 (97)	10.15	1.22 (0.99–1.52)	56.00	1.12 (0.95-1.52)	
	2.5 ki	n buffer al	round the aluminum	smelter		
SO ₂ (p.p.b.)					/>	
0-4 ^g 0-<2	551 (126) 401 (92)	10.72 10.95	1.05 (0.88–1.25) 0.95 (0.74–1.21)	48.00 48.00	0.99 (0.78–1.25) 0.93 (0.7–1.22)	
0-<2 2-4	150 (34)	9.51	1.19 (0.92–1.55)	49.00	1.16 (0.76–1.78)	
DM (us/m					. ,	
PM _{2.5} (μg/m 0–4 ^h	502 (115)	15.08	1.04 (0.88–1.22)	55.12	0.99 (0.86-1.14)	
0-<2	365 (84)	14.85	0.98 (0.81–1.20)	54.00	0.96 (0.8–1.14)	
2–4	137 (31)	15.69	1.22 (0.87–1.69)	57.00	1.05 (0.82–1.35)	

(C) 7.5 km buffer around the aluminum smelter							
SO ₂ (p.p.b.)	/10/11/10	aner aree		Sincice			
0-4 ^a	1649 (375)	9.24	1.01 (0.93-1.09)	46.00	1.03 (0.92-1.14)		
0-<2	1206 (274)	9.68	0.97 (0.88–1.07)	48.00	1.01 (0.89–1.15)		
2–4	443 (101)	8.02	1.08 (0.96–1.23)	42.00	1.09 (0.89–1.35)		
РМ _{2.5} (µg/m ³) 0-4 ^b							
0-4 b	1531 (349)	15.04	1.01 (0.93-1.11)	57.00	1.02 (0.94-1.10)		
0-<2	1137 (259)	14.28	0.94 (0.84-1.06)	56.75	0.97 (0.88-1.06)		
2–4	394 (90)	15.75	1.23 (1.02–1.48)	57.00	1.20 (1.01–1.43)		

^a27 cases (i.e., 27 case days + 111 controls days) were excluded due to missing meteorological data in case-crossover strata. ^b64 cases (i.e., 64 case days + 282 controls days) were excluded due to missing meteorological data in case-crossover strata. ^c7 cases (i.e., 7 case days + 29 control days) were excluded from analysis due to missing SO₂ data in strata ^d18 cases (i.e., 18 case days + 79 control days) were excluded from analysis due to missing PM_{2.5} data in strata. ^{e16} cases (i.e., 16 case days + 65 controls days) were excluded due to missing meteorological data in case-crossover strata. ^{f4}9 cases (i.e., 49 case days + 212 controls days) were excluded due to missing meteorological data in case-crossover strata. ^{g4} cases (i.e., 4 case days + 16 control days) were excluded from analysis due to missing SO₂ data in strata. ^{h15} cases (i.e., 15 case days + 65 control days) were excluded from analysis due to missing PM_{2.5} data in strata.

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