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ORIGINAL RESEARCH

Air Pollution and Emergency Department Visits for Suicide Attempts in Vancouver, Canada

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Abstract

Background: Comorbidity of depression, heart disease, and migraine has been observed in clinical practice, while ambient air pollution has been identified among different risk factors for these health conditions. Suicide attempts and ideations as the result of depression may be linked to air pollution exposure. Therefore the effects of ambient air pollution on emergency department (ED) visits for suicide attempts were investigated.

Methods: Emergency visit data were collected in a hospital in Vancouver, Canada. The generalized linear mixed models technique was applied in the analysis of these data. A natural hierarchical structure of the data was used to define the clusters, with days nested in a 3-level structure (day of week, month, year). Poisson models were fitted to the clustered counts of ED visits with a single air pollutant, temperature and relative humidity. In addition, the case-crossover methodology was used with the same data for comparison. The analysis was performed by gender (all, males, females) and month (all: January–December, warm: April–September, cold: October–March).

Results: Both hierarchical and case-crossover methods confirmed positive and statistically significant associations among carbon monoxide (CO), nitrogen dioxide (NO_2), sulphur dioxide (SO_2), and particulate matter (PM_{10}) for all suicide attempts in the cold period. The largest increase was observed for males in the cold period for a 1-day lagged exposure to NO_2, with an excess risk of 23.9% (95% CI: 7.8, 42.4) and odds ratio of 1.21 (95% CI: 1.03, 1.41). In warm months the associations were not statistically significant, and the highest positive value was obtained for ozone lagged by 1 day.

Conclusion: The results indicate a potential association between air pollution and emergency department visits for suicide attempts.

Keywords: air pollution, emergency department, relative humidity, suicide attempt, temperature

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Introduction

Most studies have found that suicide incidence tends to peak during spring and early summer,[1,2] a phenomenon already recognized by statisticians more than one hundred years ago.[3] The mechanism underlying the seasonality of suicide incidence is still unclear and many different factors are likely involved. Recent studies suggest that exposure to solar radiation may be an important factor.[4,5] A comprehensive review pointed out that many different methodologies have provided similar results for climate-suicide associations.[6]

Suicide attempts or death resulting from suicide are usually an outcome of mental disorder,[7] and such disorders might be affected by air pollutants. Supporting this notion is the mounting toxicological evidence from experimental animal studies showing that exposure to gaseous and particulate air pollutants can cause adverse neurological effects ranging from behavioural changes to neurodegeneration. A recent study has shown a tentative link between ozone levels and suicidal behaviour in humans,[8] while another showed an association between carbon monoxide and acute depressive episodes.[9] Positive and statistically significant results were obtained in each of these studies. The most recent study[10] associated suicide deaths with exposure to ambient particulate matter, and the strongest associations (expressed by odds ratios) were observed for persons with underlying cardiac conditions.

We propose the use of generalized linear mixed models, a relatively new statistical approach, to investigate the relationship between exposure to ambient conditions and the number of emergency department (ED) visits for suicide attempts. The case-crossover technique has also been applied as a second statistical method for comparison. Here we consider ambient air pollution and weather as an exposure and emergency department visits for suicide attempts or suicide ideation as health outcomes. Our hypothesis is that the counts of these visits are related to ambient air conditions. Our study is based on four years and two months of daily summarized counts of ED visits for suicide attempts, taking into account meteorological factors. ED data were linked to concentrations of ambient air pollutants and weather variables. We constructed models for different air pollutants: gases (carbon monoxide (CO), nitrogen dioxide (NO_2), sulphur dioxide (SO_2)) and particulate matter ($PM_{2.5}$ and PM_{10}—particulate matter with aerodynamic diameters less than 2.5 and 10 μm, respectively). In the constructed models we adjusted for weather factors.

Materials and Methods

Emergency department visits data

The study population is composed of patients served by the emergency department of St. Paul's Hospital in Vancouver, Canada. St. Paul's Hospital Emergency Department is located downtown and services the inner city population; although it does not accept trauma referrals it has a high volume (55,000/year). The study focused on emergency department visits between January 1, 1999 and February 28, 2003. 194,443 of 199,362 total visits received a viable discharge diagnosis in discharge in this 1520-day time period.

The health outcomes in the study were diagnosed ED visits identified by the standard and unique string ("SUICIDE ATTEMPT/IDEATION"). In addition, ED visits coded at the hospital as "Mental health" complaints were retrieved and analyzed. There were 9,358 ED visits with this classification. Complaint categories were accessible from July 8, 1999 onward. They were unavailable for the first six months of the study period in the database that was used (missing values). As suicide attempts or ideation might be the result of mental disorder it is reasonable to examine the association between air pollution and "Mental health" complaints.

Environmental data

Hourly air pollution data from fixed monitoring stations in Vancouver were obtained from Environment Canada. The pollutants considered in the analysis were NO_2, SO_2, O_3, CO, PM_{10}, and $PM_{2.5}$. Air pollution hourly values were used to calculate daily means, and an average among monitors was used to define a daily shared exposure. The same exposure is used for all subjects in the study and hence is called a "shared" exposure series. This is an assumption that each person in the study has the same ambient exposure.

Meteorological data were obtained from Environment Canada for the period between January 1, 1999 and February 28, 2003. Daily temperature and relative humidity were calculated as an average among 24 hour readings. We used daily mean values and their 1-day and 2-day lagged values.

Statistical analysis

We applied the generalized linear mixed models (GLMM) technique on clusters.[11] This technique has already been proposed for use in the air pollution research domain.[12] We constructed clusters based on a natural relation of the days in the data. Days of the same day of the week in the same month and year are used to segregate the original data into clusters. A cluster may contain 4 or 5 days. Poisson mixed models were applied to analyze the resulting clustered counts. The independent variables in the constructed models were air pollutant, temperature and relative humidity, taken on the same day and 1- and 2-day lagged values. We considered 3-level hierarchical formulations for random effects, whereby clusters from the same month contain month-specific random effects and clusters from the same year contain random year effects. We assumed a fixed slope and random intercept in the constructed models. The random intercept allows adjusting for different levels of counts on the clusters, and absorbs cycles and trends in time-series of the data. The method is refereed as hierarchical.

To realize our models we used the freely available R statistical software.[13] From this software the *glmmPQL* function was applied. The data used were: daily counts of visits for suicide attempts and ideation, daily averages of pollutant levels, temperature, relative humidity, and date (day, month, and year). Temperature and relative humidity were added to the constructed models as natural spline functions with 3 degrees of freedom to adjust them in the models in a nonlinear form. We conducted separate analyses for the whole period (January–December), warm months (April–September) and cold months (October–March) for same day, 1-day and 2-day lagged values.

In addition we used the case-crossover technique with a time-stratified approach to determine the controls corresponding to cases.[14,15] This analysis was conducted using the PHREG routine.[16] In the constructed models for the case-crossover technique we used the same approach as proposed by Franklin and colleagues in their analysis of $PM_{2.5}$ and mortality in 27 communities.[17] In this situation, control days for a particular case were chosen to be every third day within the same month and year that ED visit occurred. Day of the week was included in the model as an indicator variable. In this model temperature and relative humidity were included as a quadratic spline on the day of and the day before visit.

Results

Results are presented in the form of four tables and one figure. There are 1,605 visits classified in discharge with the description "SUICIDE ATTEMPT/IDEATION". The hospital used standardized character strings to identify the causes of ED diagnosed visits. The visits for suicide attempts represented 0.8% of all visits, with a mean value of 1.1 visits per day and a standard deviation of 1.1. The maximum noted number of visits per day was 9. Table 1 shows the number of visits by gender and age group. The table demonstrates that 65% (n = 1,042) of all patients were male, and 61.3% (n = 985) of cases occurred among patients younger than 40 years of age. The percentages of all visits per day of the week starting from Sunday were 13.4, 13.9, 15.8, 14.4, 15.3, 12.9 and 14.3%, respectively. In July was 10.0% (in June 9.7%) and in February and December was 6.9% of all visits. Table 2 presents some characteristics of ambient conditions in Vancouver. The presented interquartile range (IQR) for daily mean values was used to report the percentage changes in relative risks (%RR = (RR – 1) * 100%, where RR is the relative risk).

Table 3 shows the results for two periods: whole (January–December) and cold (October–March). The estimated values of excess risks (%RR) and odds ratios (OR) for each air pollutant are presented with 95% confidence intervals (95% CI). Results are shown for three types of exposure: same day, 1-day and 2-day lagged exposures. The results demonstrate positive

Table 1. Frequency of emergency department visits for suicide attempt (attempt) by age group and sex. Vancouver: January 1, 1999–February 28, 2003.

Age	Attempt	%	Female	Male
<10	7	0.4	4	3
(10, 20)	74	4.6	42	32
(20, 30)	369	23.0	154	215
(30, 40)	535	33.3	145	390
(40, 50)	386	24.0	144	242
(50, 60)	162	10.1	53	109
(60, 70)	48	3.0	10	38
(70, 80)	16	1.0	7	9
≥80	8	0.5	4	4
Total	**1,605**	**100**	**563**	**1,042**

Table 2. Daily mean, standard deviation (SD), interquartile range (IQR) for temperature, relative humidity and air pollutants. Vancouver: January 1, 1999–February 28, 2003.

Variable (unit)	Mean	SD	IQR
Weather parameters			
Temperature (°C)	7.7	11.4	8.6
Relative humidity (%)	70.7	12.5	13.4
Air pollutants			
CO (ppm)	0.5	0.2	0.2
NO_2 (ppb)	19.4	7.6	6.1
SO_2 (ppb)	6.1	4.8	1.9
O_3 (ppb)	18.3	9.5	10.9
PM_{10} (μg/m^3)	25.8	14.2	6.9
$PM_{2.5}$ (μg/m^3)	8.6	6.7	5.1

and statistically significant associations between ED visits for suicide attempts and exposure to CO, NO_2, SO_2, PM_{10} and PM_{25}. The table contains only results with a *P*-value of not greater than 0.05 (for%RR).

The presented figure shows the results (%RR) for the whole, cold (October–March), and warm (April–September) periods. There are no positive and statistically significant results for warm period (April–September). Figure 1 shows all the results by sex and season.

In addition, ED visits coded at the hospital as "Mental health" complaints were retrieved and analyzed. Table 4 replicates Table 3 with ED visits for "Mental health" complaints as the health outcome instead of ED diagnosed visits for suicide attempts. The table was constructed for the same pollutants and their corresponding lags. Of ED visits classified in discharge with the description "SUICIDE ATTEMPT/IDEATION", 86.5% declared mental health complaints upon entrance. This analysis affords an increase in sample size and allows the investigation of similarities in responses to exposures.

Discussion

This study examined visits for suicide attempts in a single ED in Vancouver and linked them to environmental conditions, especially air quality, in close proximity to the suicide attempt. The main result of this study is the demonstration of an association between exposure to air pollution and the numbers of ED visits for suicide attempts.

It should be noted that the dependency of ED visits on air pollutants as presented in this and other papers is purely a statistical association. As such the results cannot be treated as proof of the thesis that air pollution may trigger suicidal behaviour.[5,18] The results also show that the association between ambient air pollution concentrations and ED visits for suicide

Table 3. The percentage changes in the relative risk (%RR) and odds ratio (OR) with the corresponding 95% confidence intervals (95% CI) for ED visits for suicide attempt, in relation to an increase in the IQR of ambient air pollutants in Vancouver.

Method			Hierarchical		Case-crossover	
Pollutant	**lag**	**Period, sex**	**%RR**	**95% CI**	**OR**	**95% CI**
CO	0	All, male	9.6	0.9, 19.2	1.07	0.99, 1.15
CO	0	Cold, all	11.8	3.7, 20.6	1.07	1.01, 1.14
CO	0	Cold, male	15.0	5.1, 25.9	1.10	1.01, 1.19
CO	1	Cold, all	9.2	1.3, 17.7	1.06	0.99, 1.13
CO	1	Cold, male	13.4	3.6, 24.0	1.07	0.98, 1.16
CO	1	All, male	10.3	1.5, 19.9	1.06	0.99, 1.14
NO_2	0	Cold, all	16.2	3.5, 30.3	1.12	1.00, 1.27
NO_2	0	Cold, male	17.3	2.1, 34.7	1.16	1.00, 1.35
NO_2	1	Cold, all	15.4	2.9, 29.5	1.17	1.04, 1.33
NO_2	1	Cold, male	23.9	7.8, 42.4	1.21	1.03, 1.41
NO_2	1	All, male	11.2	0.6, 22.8	1.11	1.00, 1.22
NO_2	2	Cold, male	19.7	3.9, 37.8	1.17	1.03, 1.35
SO_2	0	Cold, all	10.9	1.3, 21.5	1.07	0.98, 1.16
PM_{10}	0	Cold, all	13.2	1.9, 25.8	1.11	1.00, 1.23
PM_{10}	1	Cold, male	15.0	1.4, 30.4	1.11	0.97, 1.26
$PM_{2.5}$	0	Cold, male	16.0	1.2, 33.0	1.10	0.97, 1.26
$PM_{2.5}$	1	Cold, male	15.5	0.7, 32.4	1.09	0.95, 1.25

Note: IQR = 75th–25th percentiles.

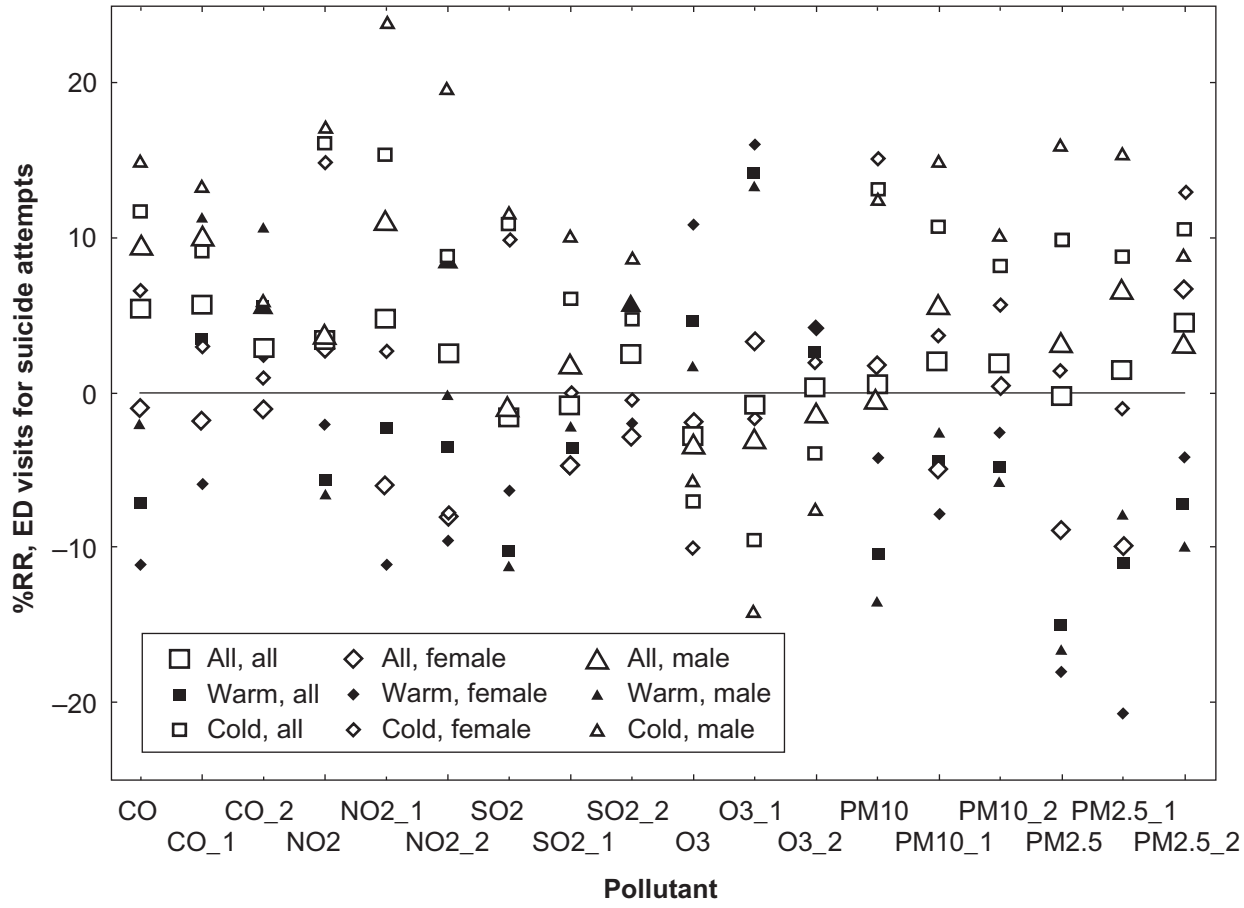

Figure 1. The excess risks (%RR) for an increase of the IQR for pollutants and their lags (0–2 days) by sex and period.

attempts or ideation appears to be stronger when the weather is colder.

The results for exposure to ozone (see Fig. 1) agree with those presented in work by Biermann et al.[8] The statistical methods used (hierarchical and case-crossover) in each case provided consistent results. For some configurations of exposure/sex/period, the case-crossover models were more restrictive and showed only positive associations (see Table 3). Both methods confirm statistically significant positive results for CO, NO_2 and PM_{10} in the cold months. For ED visits for mental conditions (complaints, ie, non-diagnosed), CO and NO_2 again show associations. The positive association for sulphur dioxide is interesting as it agrees with previous observations for female ED visits for migraine[19] and associations with female visits for depression.[20] Vancouver is a relatively warm city compared with other Canadian cities. Those associations were observed for all months and cold months, but not for warm months, may be due to specific environmental influences.

Recent epidemiologic research has found that occupational exposure to pesticides is positively associated with suicide risk.[21–23] In the occupational exposure concentrations of pollutants are much higher than in considered here ambient air pollution exposures. Animal studies have linked organophosphate exposure to serotonin disturbances in the central nervous system (CNS), which are implicated in depression and suicide in humans.[24] These data provide supporting evidence that pollutant exposure may be a factor in depression, suicide or related outcomes in human populations.[20,25,26]

There is mounting toxicological evidence that gaseous and particulate air pollutants can adversely affect the brain and nervous system. Brain damage and severe neuropsychiatric symptoms can result from acute carbon monoxide (CO) intoxication. At lower doses, CO exposure can lead to vision problems and decrements in hand-eye coordination and attention/vigilance, influencing manual dexterity, the performance of complex tasks, and the ability to work or

Table 4. The percentage changes in relative risk (%RR) with the corresponding 95% confidence intervals (95% CI) for ED visits for mental health (complaints), in relation to an increase in the IQR of ambient air pollutants in Vancouver.

Patients	All		Male		Female	
Pollutant, period	**%RR**	**95% CI**	**%RR**	**95% CI**	**%RR**	**95% CI**
CO, all	2.7	0.2, 5.2	2.4	–0.7, 5.6	3.4	–0.8, 7.7
CO, cold	3.2	0.4, 6.1	3.1	–0.3, 6.7	3.9	–0.9, 8.9
CO-1, all	0.4	–2.1, 2.9	0.9	–2.1, 4.1	–0.4	–4.5, 3.8
CO-1, cold	1.7	–1.1, 4.5	1.9	–1.5, 5.5	1.4	–3.3, 6.3
NO_2, cold	6.3	1.5, 11.4	5.5	–0.3, 11.7	7.8	–0.6, 16.8
NO_2-1, all	0.3	–3.0, 3.7	0.2	–3.8, 4.5	0.6	–4.9, 6.4
NO_2-1, cold	3.0	–1.7, 7.9	2.8	–3.0, 9.0	3.3	–4.7, 11.9
NO_2-2, cold	–1.9	–6.4, 2.8	–0.8	–6.4, 5.2	–3.9	–11.4, 4.3
SO_2, cold	5.1	1.2, 9.1	4.2	–0.3, 9.1	7.3	0.8, 14.1
PM_{10}, cold	3.7	–0.6, 8.2	3.1	–2.2, 8.7	5.8	–1.8, 14
PM_{10}-1, cold	2.1	–2.2, 6.5	4.0	–1.3, 9.6	–1.0	–8.1, 6.7
$PM_{2.5}$, cold	4.3	–0.8, 9.8	4.1	–2.1, 10.7	5.6	–3.5, 15.4
$PM_{2.5}$-1, cold	2.0	–3.2, 7.4	4.0	–2.2, 10.6	–2.5	–10.8, 6.6

Note: Air pollutants lagged by n days (CO-1; ie. CO lagged by 1-day, etc.).

learn.[27] The effects of CO on the CNS are thought to be due to its interference with oxygen delivery to the brain, although the mechanism is not fully understood. Interestingly CO is also an endogenous neurotransmitter. It has become apparent that inhalation of particulate matter (PM) can impact the CNS. Recent work with experimental animals has provided evidence for neuropathological effects including reduced dopaminergic neuron density in mice exposed to concentrated ambient particles (CAPs);[28] changes in neurotransmitter levels in rats exposed to inhaled CAPs;[29] and altered inflammatory and stress protein responses in the brains of mice following pulmonary exposure to CAPs or ultrafine carbon black and in the brains of feral dogs breathing ambient Mexico City air.[30–32]

There is some evidence from studies of laboratory animals that inhaled particles, especially in the ultrafine size fraction, may be able to distribute to the brain.[33–35] However there is a lack of clinical research on PM-induced neurological effects in humans. PM is a complex mix of chemicals that can vary in time and space and may include among its constituents substances that are directly neurotoxic, for example VOCs and metals such as manganese and lead. The extent of impact on human populations of neurotoxic PM components at levels typically found in ambient air is generally not known. Overall there is a growing toxicologic database showing that exposure to gaseous and particulate air pollutants can cause adverse neurological effects ranging from behavioural changes to neurodegeneration. This evidence, mainly from experimental animal studies, provides a biological plausibility to the notion that exposure of human populations to air pollutants, in concert with susceptibility factors related to age, disease or genetics, may result in neurochemical or neuropathological changes that could potentially manifest as or contribute to depression, suicide ideation or related psychological outcomes.[20,36]

We should mention the recent publication on the relation between weather and suicide,[37] which suggests a link between industry chemicals and increased suicide rates,[38] and multi-city study on ED visits for depression in Canada.[39]

There are limitations in the interpretation of the findings of this study that are typical of this type of research, including the adequacy of the model and the impact of measurement error in the exposure and outcome variables. Another limitation is the assumption that each person has the same exposure. Misclassification of cause of ED visits or underreporting in the hospital registry system might have confounded the results. The number of visits per day is low, and mortality data on suicide deaths would likely be more adequate for this type of study. It should be noted that the presented results are based on a statistical methodology that has a long history and is well accepted among researchers. The proposed approach is a new technique for assessing the impact of ambient conditions on health outcomes.

The results show that exposure to air pollutants, such as carbon monoxide, nitrogen dioxide, sulphur dioxide and particulate matter, may be associated with the numbers of ED visits for suicide attempts.

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Disclosure

This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers of this paper report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material.

References

1. Petridou E, Papadopoulos FC, Frangakis CE, Skalkidou A, Trichopoulos D. A role of sunshine in the triggering of suicide. *Epidemiology*. 2002;13: 106–9.
2. Partonen T, Haukka J, Nevanlinna H, Lönnqvist J. Analysis of the seasonal pattern in suicide. *J Affect Disord*. 2004;81:133–9.
3. Durkheim E. Le suicide/Der Selbstmort. (In French/German). *Frankfurt*. Germany: Suhrkamp Verlag; 1897/1983.
4. Papadopoulos FC, Frangakis CE, Skalkidou A, Petridou E, Stevens RG, Trichopoulos D. Exploring lag and duration effect of sunshine in triggering suicide. *J Affect Disord*. 2005;88:287–97.
5. Ajdacic-Gross V, Lauber C, Sansossio R, et al. Seasonal associations between weather conditions and suicide-evidence against a classic hypothesis. *Am J Epidemiol*. 2007;165:561–9.
6. Deisenhammer EA. Weather and suicide: the present state of knowledge on the association of meteorological factors with suicidal behaviour. *Acta Psychiatr Scand*. 2003;108:402–9.
7. Harris EC, Barraclough B. Suicide as an outcome for mental disorders. *A meta-analysis Br J Psychiatry*. 1997;170:2005–228.
8. Biermann T, Stilianakis N, Bleich S, Thürauf N, Kornhuber J, Reulbach U. The hypothesis of an impact of ozone on the occurrence of completed and attempted suicides. *Med Hypotheses*. 2009;72(3):338–41.
9. Szyszkowicz M. Air pollution and emergency department visits for depression in Edmonton, Canada. *Int J Occup Med Environ Health*. 2007; 20(3):241–5.
10. Changsoo K, Sang HJ, Dae RK, et al. Ambient particulate matter as a risk factor for suicide. *Amer J Psychiatry*. 2010 (AJP in Advance, doi: 10.1176/appi.ajp.2010.09050706).
11. Molenberghs G, Verbeke G. Models for discrete longitudinal data. New York: Springer; 2005.
12. Szyszkowicz M. Use of generalized linear mixed models to examine the association between air pollution and health outcomes. *Int J Occup Med Environ Health*. 2006;19:224–7.
13. R-2.6.2. R Development Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, Austria. URL: http://www.r-project.org, (Accessed on 2008 Apr 29).
14. Maclure M. The case-crossover design. A method for studying transient effects on the risk of acute events. *Am J Epidemiol*. 1991;133: 144–53.
15. Janes H, Sheppard L, Lumley T. Case-crossover analyses of air pollution exposure data. Referent selection strategies and their implications for bias. *Epidemiology*. 2005;16:717–26.
16. SAS Institute Inc. SAS Version 9.1. Cary, North Carolina, 2002.
17. Franklin M, Zeka A, Schwartz J. Association between $PM_{2.5}$ and all-cause and specific-cause mortality in 27 US communities. *Journal of Exposure Science and Environmental Epidemiology*. 2007;17:279–87.
18. Lee HC, Lin HC, Tsai SY, Li CY, Chen CC Huang CC. Suicide rates and the association with climate: a population-based study. *J Affect Disord*. 2006; 92:221–6.
19. Szyszkowicz M, Rowe BH, Kaplan GG. Ambient sulphur dioxide exposure and emergency department visits for migraine in Vancouver, Canada. *Int J Occup Med Environ Health*. 2009;22(1):7–12.
20. Szyszkowicz M. Ambient sulfur dioxide and female ED visits for depression. Air Quality, Atmosphere and Health. 2010; doi: 10.1007/s11869-010-0081-8.
21. Lee WJ, Alavanja MCR, Hoppin JA, et al. Mortality among pesticide applicators exposed to chlorpyrifos in the Agricultural Health Study. *Environ Health Perspect*. 2007;115:528–34.
22. Stallones L. Suicide and potential occupational exposure to pesticides, Colorado 1990–1999. *Journal-of-Agromedicine*. 2006;11:107–12.
23. van Wijngaarden E. An exploratory investigation of suicide and occupational exposure. *J Occup Environ Med*. 2003;45:96–101.
24. London L, Flisher AJ, Wesseling C, Mergler D, Kromhout H. Suicide and exposure to organophosphate insecticides: cause or effect? *Am J Ind Med*. 2005;47:308–21.
25. Cleland JA, Lee AJ, Hall S. Associations of depression and anxiety with gender, age, health-related quality of life and symptoms in primary care COPD patients. *Fam Pract*. 2007;24:217–23.
26. di Marco F, Verga M, Reggente M, et al. Anxiety and depression in COPD patients: The roles of gender and disease severity. *Respir Med*. 2006;100:1767–74.
27. Raub JA, Benignus VA. Carbon Monoxide and the Nervous System. *Neuroscience and Behavioral Reviews*. 2002;26:925–40.
28. Veronesi B, Makwana O, Pooler M, Chen LC. Effects of subchronic exposures to concentrated ambient particles. VII. Degeneration of dopaminergic neurons in Apo E-/- mice. *Inhal Toxicol*. 2005;17:235–41.
29. Sirivelu MP, MohanKumar SM, Wagner JG, Harkema JR, MohanKumar PS. Activation of the stress axis and neurochemical alterations in specific brain areas by concentrated ambient particle exposure with concomitant allergic airway disease. *Environ Health Perspect*. 2006;114:870–4.
30. Campbell A, Oldham M, Becaria A, et al. Particulate matter in polluted air may increase biomarkers of inflammation in mouse brain. *Neurotoxicology*. 2005;26:133–40.
31. Shwe TTW, Yamamoto S, Ahmed S, Kakeyama M, Kobayashi T, Fujimaki H. Brain cytokine and chemokine mRNA expression in mice induced by intranasal instillation with ultrafine carbon black. *Toxicology Letters*. 2006;163:153–60.
32. Calderon-Garciduenas L, Maronpot RR, Torres-Jardon R, et al. DNA damage in nasal and brain tissues of canines exposed to air pollutants is associated with evidence of chronic brain inflammation and neurodegeneration. *Toxicol Pathol*. 2003;31:524–38.
33. Kreyling WG, Semmler M, Erbe F, et al. Translocation of ultrafine insoluble iridium particles from lung epithelium to extrapulmonary organs is size dependent but very low. *J Toxicol Environ Health*. A 2002;65: 1513–30.
34. Oberdörster G, Sharp Z, Atudorei V, et al. Translocation of inhaled ultrafine particles to the brain. *Inhal Toxicol*. 2004;16:437–45.

35. Peters A, Veronesi B, Calderon-Garciduenas L, et al. Translocation and potential neurological effects of fine and ultrafine particles a critical update. *Part-Fibre-Toxicol*. 2006;3:13.
36. Brådvik L, Mattisson C, Bogren M, Nettelbladt P. Mental disorders in suicide and undetermined death in the lundby study. The contribution of severe depression and alcohol dependence. *Arch Suicide Res*. 2010;14:266–75.
37. Töro K, Dunay G, Bartholy J, Pongrácz R, Kis Z, Keller E. Relationship between suicidal cases and meteorological conditions. *J Forensic Leg Med*. 2009 Jul;16(5):277–9.
38. University of North Carolina School of Medicine (2005, Nov 14). Increased suicide rate with possible link to nearby industry chemicals in Second N. C., community. Science Daily. Retrieved 2009 Oct 20.
39. Szyszkowicz M, Rowe B, Colman I. Air pollution and daily emergency department visits for depression. *Int J Occup Med Environ Health*. 2009; 22(4):355–62.