Outdoor Air Pollution and Stroke in Sheffield, United Kingdom
A Small-Area Level Geographical Study

Ravi Maheswaran, MD; Robert P. Haining, PhD; Paul Brindley, MSc; Jane Law, PhD; Tim Pearson, MSc; Peter R. Fryers, MSc; Stephen Wise, BSc; Michael J. Campbell, PhD

Background and Purpose—Current evidence suggests that stroke mortality and hospital admissions should be higher in areas with elevated levels of outdoor air pollution because of the combined acute and chronic exposure effects of air pollution. We examined this hypothesis using a small-area level ecological correlation study.

Methods—We used 1030 census enumeration districts as the unit of analysis and examined stroke deaths and hospital admissions from 1994 to 1998, with census denominator counts for people ≥45 years. Modeled air pollution data for particulate matter (PM10), nitrogen oxides (NOx), and carbon monoxide (CO) were interpolated to census enumeration districts. We adjusted for age, sex, socioeconomic deprivation, and smoking prevalence.

Results—The analysis was based on 2979 deaths, 5122 admissions, and a population of 199 682. After adjustment for potential confounders, stroke mortality was 37% (95% CI, 19 to 57), 33% (95% CI, 14 to 56), and 26% (95% CI, 10 to 46) higher in the highest, relative to the lowest, NOx, PM10, and CO quintile categories, respectively. Corresponding increases in risk for admissions were 13% (95% CI, 1 to 27), 13% (95% CI, −1 to 29), and 11% (95% CI, −1 to 25).

Conclusion—The results are consistent with an excess risk of stroke mortality and, to a lesser extent, hospital admissions in areas with high outdoor air pollution levels. If causality were assumed, 11% of stroke deaths would have been attributable to outdoor air pollution. Targeting policy interventions at high pollution areas may be a feasible option for stroke prevention. (Stroke. 2005;36:239-243.)

Key Words: air pollutants, environmental cerebrovascular disorders hospitalization mortality

There is increasing evidence linking outdoor air pollution and stroke. Recent studies have found acute effects on stroke mortality and hospital admissions related to daily variation in outdoor pollution levels.1–3 Early studies reporting an association between air pollution and stroke mortality, which examined pollution episodes when pollution levels were very high, also support an acute effect.4,5 Evidence of the chronic effect of air pollution on stroke comes mainly from cohort studies examining the effect of chronic exposure to occupational and indoor sources of pollution.6–8 Three cohort studies on chronic exposure to outdoor air pollution have reported increased risks for cardiorespiratory mortality, although none specifically reported on stroke.9–11

The evidence suggests that stroke mortality and hospital admissions should be higher in areas with elevated levels of outdoor air pollution because of the combined acute and chronic exposure effects of air pollution on stroke risk. Evidence of raised stroke risk in high pollution areas would support targeting of policy interventions on such areas to reduce pollution levels. We therefore examined the hypothesis that stroke mortality and hospital admission rates are higher in areas with higher levels of outdoor air pollution, using a small-area level ecological correlation study. Small-area level studies are able to capture fine grain variation in outdoor air pollution levels. In addition, population characteristics, including exposure levels and socioeconomic factors, are likely to be more homogenous within small geographical areas.

Methods

We used 1030 census enumeration districts (CEDs) as the unit of analysis. We examined routinely collected data on stroke deaths (International Classification of Diseases, 9th Revision 430 to 438) from 1994 to 1998 from the national death registration system, and emergency hospital admissions (International Classification of Diseases, 10th Revision, I60 to I69) from April 1994 to March 1999 from the hospital episode statistics system. We used 1991 census denominator populations corrected for underenumeration12 and scaled to midyear estimates for Sheffield Health Authority by age and sex for 1994 to 1998.
Sheffield City Council provided modeled air pollution data at a 200-m grid square resolution for particulate matter (PM$_{10}$), nitrogen oxides (NO$_x$) and carbon monoxide (CO) generated using an air pollution model (Indic-Airviro, SMHI Inc). The pollution model incorporated point (eg, factories), line (eg, roads), and grid (eg, background emissions from housing estates) sources of pollution and meteorological data. Models were run for 1994 to 1999 (excluding 1998 because of incomplete meteorological data), and the 5-year average was calculated. Model validation using visual inspection of pollution maps and comparison with monitored pollution levels, and limitations of these modeled data, have been reported previously.$^{13}$

In summary, the pollution patterns on NO$_x$ and CO maps appeared valid but the PM$_{10}$ map had 6 circumscribed areas (108 CEDs) with erroneously high levels because of artifacts in the emissions database. These CEDs were therefore excluded before any statistical analysis was undertaken. The model appeared to overestimate NO$_x$ and underestimate CO levels compared with monitored levels. Modeled values were therefore rescaled to monitored equivalent values using linear regression and the analysis was carried out using categories by quintile to examine effects of relative rather than absolute pollution values.

Interpolation of pollution values to CEDs took into account population locations within CEDs using postcodes weighted by the number of domestic delivery points within each postcode, using previously described methodology.$^{14}$ To examine if estimates of the outdoor air pollution exposure effect would be improved by taking into account daily local population movements with consequent variation in exposure, average exposures using a 1-km radius around each postcode centroid were also calculated and interpolated to CEDs.$^{13}$ Surveys indicate that 1 km is the average walking journey length.$^{15}$

We used the Townsend index, a widely used deprivation index in England, to adjust for socioeconomic deprivation at the CED level.$^{16}$ This is a standardized combination of 4 1991 census variables: the proportion of economically active residents who were unemployed; the proportion of households without a car; the proportion of households not owner-occupied; and the proportion of overcrowded households.

To adjust for cigarette smoking prevalence, we used survey data from a random sample of adults (66% response) carried out in 2000. Of the 9821 respondents with complete smoking information, 2532 were smokers, giving an overall smoking prevalence of 25.8%. Ward level smoking prevalence (29 electoral wards in Sheffield) was attributed to all CEDs within each ward. (Smoking prevalence at the CED level would have been based on very small numbers.)

**Statistical Analysis**

We used Poisson regression methods in SAS.$^{17}$ We grouped CED level data by sex, age band (9 categories from 45 to 85 + years), pollutant category by quintile, deprivation category by quintile, and smoking prevalence by quintile. The effect of each of the pollutants was examined in separate analyses adjusted for age, sex, deprivation, and smoking prevalence by quintile. The inclusion of an age-by-deprivation interaction, because this has previously been found to be substantial in magnitude.$^{18}$ The results are presented as rate ratios (with 95% CIs adjusted for overdispersion). Analyses were then rerun, substituting unsmoothed pollution variables with the 1-km radius smoothed variables.

We also examined for spatial autocorrelation in model residuals between neighboring areas, which could bias results, using a conditional autoregressive spatial model.$^{19,20}$ Observed and expected counts (standardized for age, sex, and deprivation) were modeled

<table>
<thead>
<tr>
<th>Category by Quintile</th>
<th>NO$_x$ (µg/m$^3$)</th>
<th>PM$_{10}$ (µg/m$^3$)</th>
<th>CO (µg/m$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>61.9 (25.7)</td>
<td>23.3 (10.6)</td>
<td>482 (245)</td>
</tr>
<tr>
<td>4</td>
<td>55.8 (54.2–57.7)</td>
<td>19.8 (19.3–20.6)</td>
<td>443 (433–455)</td>
</tr>
<tr>
<td>3</td>
<td>53.0 (52.0–54.2)</td>
<td>18.8 (18.2–19.3)</td>
<td>426 (419–433)</td>
</tr>
<tr>
<td>2</td>
<td>50.9 (49.6–52.0)</td>
<td>17.5 (16.8–18.2)</td>
<td>405 (387–419)</td>
</tr>
<tr>
<td>1</td>
<td>47.6 (49.6)</td>
<td>16.0 (15.6)</td>
<td>360 (387)</td>
</tr>
</tbody>
</table>

**TABLE 1. Mean Values and Category Limits for Modeled NO$_x$, PM$_{10}$, and CO Levels in Sheffield, United Kingdom, 1994 to 1999**

Mean modeled NO$_x$ levels for CEDs in Sheffield, United Kingdom, 1994 to 1999.

![Image of Mean NO$_x$ levels 1994–1999](http://stroke.ahajournals.org/content/.../ figures.png)
Results
The analysis was based on 2979 deaths and 5122 emergency hospital admissions from stroke over the 5-year period for people aged ≥45 years. The corresponding denominator population was 199,682, giving on average 194 people aged ≥45 years per CED.

Modeled outdoor pollution levels within categories by quintile are shown in Table 1. NOx in the highest pollution category was 1.3× that in the lowest category, and the corresponding levels for PM10 and CO were 1.5 and 1.3, respectively. Correlation coefficients for NOx with PM10 and CO values for CEDs were 0.87 and 0.88, respectively, and 0.82 for PM10 with CO. The air pollution pattern of one of the pollutants (NOx) is shown in the Figure.

Mortality
Rate ratios for stroke mortality adjusted for age and sex, and then further adjusted for socioeconomic deprivation and smoking prevalence in relation to pollutant categories, are shown in Table 2. Rate ratios generally increased across categories, although there was some inconsistency across the lower NOx and higher CO categories. Additional adjustment for socioeconomic deprivation and smoking prevalence only marginally diminished mortality rate ratios.

After adjusting for age, sex, deprivation, and smoking prevalence, stroke mortality in the highest NOx category was 1.37× (95% CI, 1.19 to 1.57) that in the lowest category. For PM10, after adjustment for the 4 confounders, the risk of stroke mortality was 1.33 (95% CI, 1.14 to 1.56) in the highest relative to the lowest category. For CO, adjusted rate ratios in the highest and second highest categories were 1.26 (95% CI, 1.10 to 1.46) and 1.32 (95% CI, 1.15 to 1.50), respectively.

Mortality rate ratios based on 1-km radius spatially smoothed exposure estimates that take into account daily population movements are shown in Table 3. The use of smoothed pollution estimates tended to diminish rate ratios for all 3 pollutants.

Hospital Admissions
Rate ratios for stroke hospital admissions by pollutant category are shown in Table 2. Rate ratios generally increased across pollution categories but in contrast to mortality, additional adjustment for deprivation and smoking prevalence substantially diminished the magnitude of the associations.

For NOx, after adjustment for confounders, an elevated risk was still apparent, with a risk of stroke admission of 1.13 (95% CI, 1.01 to 1.27) in the highest relative to the lowest category. For PM10, the adjusted rate ratio was 1.13 (95% CI, 0.99 to 1.29) in the highest relative to the lowest category. For CO, the rate ratio was 1.11 (95% CI, 0.99 to 1.25) in the highest category.

Rate ratios based on 1-km radius smoothed exposure estimates are shown in Table 3. The smoothed exposure estimates did not appear to enhance admission rate ratios for all 3 pollutants compared with estimates based on unsmoothed pollution values.

There was no evidence of residual spatial autocorrelation for mortality or hospital admissions once age, sex, and deprivation had been accounted for.

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Mortality</th>
<th>Hospital Admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOx</td>
<td>1.46 (1.29–1.65)</td>
<td>1.40 (1.27–1.55)</td>
</tr>
<tr>
<td>PM10</td>
<td>1.30 (1.15–1.46)</td>
<td>1.23 (1.11–1.35)</td>
</tr>
<tr>
<td>CO</td>
<td>1.06 (0.94–1.20)</td>
<td>1.05 (0.95–1.16)</td>
</tr>
</tbody>
</table>

TABLE 2. Rate Ratios for Mortality and Emergency Hospital Admissions Because of Stroke in Relation to Modeled Outdoor Air Pollution (NOx, PM10, and CO) Categories by Quintile in Sheffield, United Kingdom, 1994 to 1998

<table>
<thead>
<tr>
<th>Pollutant</th>
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<th>Hospital Admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOx</td>
<td>1.37 (1.19–1.57)</td>
<td>1.13 (1.01–1.27)</td>
</tr>
<tr>
<td>PM10</td>
<td>1.20 (1.06–1.36)</td>
<td>1.05 (0.94–1.16)</td>
</tr>
<tr>
<td>CO</td>
<td>1.04 (0.91–1.18)</td>
<td>0.93 (0.84–1.03)</td>
</tr>
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<tr>
<th>Pollutant</th>
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<th>Hospital Admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOx</td>
<td>1.39 (1.23–1.58)</td>
<td>1.40 (1.26–1.55)</td>
</tr>
<tr>
<td>PM10</td>
<td>1.16 (1.03–1.32)</td>
<td>1.25 (1.12–1.38)</td>
</tr>
<tr>
<td>CO</td>
<td>1.12 (0.99–1.27)</td>
<td>1.10 (0.99–1.23)</td>
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</table>

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<tr>
<th>Pollutant</th>
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</thead>
<tbody>
<tr>
<td>NOx</td>
<td>0.95 (0.84–1.08)</td>
<td>1.06 (0.95–1.17)</td>
</tr>
<tr>
<td>PM10</td>
<td>1.09 (0.96–1.24)</td>
<td>1.02 (0.92–1.12)</td>
</tr>
<tr>
<td>CO</td>
<td>1.04 (0.91–1.13)</td>
<td>1.01 (0.99–1.13)</td>
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<tbody>
<tr>
<td>NOx</td>
<td>1.33 (1.14–1.56)</td>
<td>1.13 (0.99–1.29)</td>
</tr>
<tr>
<td>PM10</td>
<td>1.12 (0.97–1.29)</td>
<td>1.08 (0.96–1.22)</td>
</tr>
<tr>
<td>CO</td>
<td>1.08 (0.94–1.24)</td>
<td>0.98 (0.87–1.10)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Mortality</th>
<th>Hospital Admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOx</td>
<td>0.94 (0.83–1.07)</td>
<td>1.01 (0.91–1.13)</td>
</tr>
<tr>
<td>PM10</td>
<td>1.04 (0.91–1.13)</td>
<td>1.00 (0.90–1.12)</td>
</tr>
<tr>
<td>CO</td>
<td>1.04 (0.91–1.13)</td>
<td>1.00 (0.90–1.12)</td>
</tr>
</tbody>
</table>
Discussion

After adjusting for age, sex, socioeconomic deprivation, and smoking prevalence, we found that increasing outdoor air pollution levels were significantly associated with increasing stroke mortality risk at the small-area level. Spatially smoothed pollution estimates did not enhance observed rate ratios. The associations between outdoor air pollution and hospital admissions from stroke were smaller in magnitude and of borderline significance. The results are consistent with an excess risk of stroke mortality and, to a lesser extent, an excess risk of stroke emergency hospital admissions in areas with high outdoor air pollution levels.

One previous study has examined the association between stroke mortality and air pollution at the small-area level. Proximity to main roads was used as a proxy for exposure to road traffic pollution, and a 5% increase in stroke mortality was observed in areas within 200 m of a main road. Chronic exposure to indoor air pollution from coal burning was associated with a stroke mortality relative risk of 2.55, whereas studies examining chronic occupational exposure to air pollutants reported relative risks of 1.43 to 3.1. Two cohort studies on outdoor air pollution reported relative risks of 1.26 to 1.37 for the most polluted areas for cardiorespiratory mortality. Another reported a relative risk of 1.95 for cardiorespiratory mortality associated with living near a major road. A further cohort study examined cause-specific mortality and observed a nonsignificant relative risk of 1.04 for stroke for a 10 μg/m³ increase in NOx.

A number of potential mechanisms could explain the association between air pollution and stroke. It has been hypothesized that fine particulate air pollution provokes alveolar inflammation, causing the release of potentially harmful cytokines, which results in increased coagulability. Experimental evidence suggests that ultrafine particles are able to penetrate the human lung and enter the blood circulation. Particulate air pollution has been shown to induce progression of atherosclerosis in an animal model. Abnormal function of vascular endothelial cells has been implicated in early atherogenesis, and studies have demonstrated inhibition of endothelium-dependent vasorelaxation by automotive exhaust particles. Another less clearly delineated potential mechanism may operate through the association between impaired lung function and stroke as a consequence of the adverse effects of chronic exposure to air pollution on lung function.

There was a clearer effect of outdoor air pollution on stroke mortality than on emergency hospital admissions. A similar observation has been reported previously in relation to the winter effect on cardiovascular disease, where there was clear evidence of excess deaths in winter but no evidence of association with emergency hospital admissions. One possible explanation is that even emergency hospital admissions for stroke are influenced by a number of other factors, and these could have masked the air pollution effect. Another is that the air pollution effect is more likely to result in fatal stroke.

A number of potential limitations to this study need to be considered. As this was an ecological study, the potential for ecological bias (ie, the situation where the association seen at the group level may be different from that which exists at the individual level) cannot be ruled out. However, this may be less of a problem with small-area level ecological studies. There is also potential for exposure misclassification because...
of limitations regarding exposure modeling. However, area-level exposure misclassification may have diluted the magnitude of the association at the ecological level. The contrast between high- and low-pollution areas was small compared with the 6 cities study, for example.6 Explanations include smaller within-city variation, the averaging effect of interpolation to CEDs, and regression attenuation when modeled values were rescaled to monitored equivalent values, with greater attenuation for CO and NO\textsubscript{x} than PM\textsubscript{10}. We did not take into account long-term population moves, and this potential source of exposure misclassification could lead to an underestimation of the underlying association. There may have been errors in death certification and diagnosis and coding of hospital admissions which could also have diluted the magnitude of any underlying association. We did not examine 2 or 3 pollutant models because of the high degree of correlation between all 3 pollutants. Although we adjusted for socioeconomic deprivation and smoking prevalence at the area level, residual confounding because of these factors cannot be ruled out. However, adjustment for these factors made a relatively small change in effect estimates for mortality. We had no data on hypertension prevalence or other stroke risk factors that could potentially have confounded the associations observed. We did not examine stroke subtypes. The air pollution effect might be confined to ischemic stroke and further work is required to examine this aspect.

If we assume causality and use NO\textsubscript{x} as an indicator of outdoor air pollution, 11% of stroke deaths in Sheffield would have been attributable to the adverse effects of outdoor air pollution. Although this population attributable risk fraction is not large, outdoor air pollution is important, because it is a potentially modifiable risk factor for stroke. Our results suggest that targeting policy interventions at high pollution areas may be a feasible option for stroke prevention. Further studies are needed to confirm our findings, incorporating individual level information to adjust for potential confounding factors.

Acknowledgments
This study was funded by a grant from the Trent Research Scheme. The views expressed in this article are those of the authors and not necessarily those of the funding organization. This work uses data provided with the support of the Economic and Social Research Council (ESRC) and Joint Information Systems Committee (JISC) and census and boundary material, which are copyright of the Crown, the Post Office, and the ED-LINE Consortium.

References
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*Stroke*. 2005;36:239-243; originally published online December 16, 2004; doi: 10.1161/01.STR.0000151363.71221.12

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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