



# Correcting for the effects of location and atmospheric conditions on air pollution exposures in a case–crossover study

LIANNE SHEPPARD,<sup>a</sup> DREW LEVY<sup>b</sup> AND HARVEY CHECKOWAY<sup>c</sup>

<sup>a</sup>Departments of Biostatistics and Environmental Health, University of Washington, Seattle, Washington 98195-7232

<sup>b</sup>Department of Epidemiology, University of Washington, Seattle, Washington 98195-7232

<sup>c</sup>Departments of Environmental Health and Epidemiology, University of Washington, Seattle, Washington 98195-7232

A limitation of most air pollution health effects studies is that they rely on monitoring data averaged over one or more ambient monitors to represent daily air pollution exposures for individuals. Such data analyses therefore implicitly require the assumption of a homogeneous spatial distribution for particulate matter (PM). This assumption may be suspected in the Pacific Northwest because of its hilly topography and local variations in wood burning. To examine the bias from substituting regional PM (i.e., the average of three ambient monitor measurements) for individual PM exposure, we conducted an exposure substudy to identify the influence of location factors, specifically urban *versus* suburban classification and topographic features (“upstream” *versus* “downstream”), on local ambient measurements. Using nephelometer measurements collected over 1 year in four locations, we developed regression models to predict local PM as a function of regional PM, atmospheric stagnation, temperature, and location. We found a significant interaction between atmospheric stagnation and topography, with the most upstream site having reduced PM levels on high stagnation days after controlling for regional PM. We also found a significant interaction with temperature at one downstream site thought to be heavily exposed to wood smoke in the winter. These results are consistent with the physics of surface radiation inversions. The interactions reordered the index *versus* referent exposures in a case–crossover analysis of out-of-hospital primary cardiac arrest for subjects living in specific locations, but did not meaningfully change the associations with PM from the analysis using regional PM as the exposure. The lack of change in these results may be due to limitations in the data used to correct the exposure estimates or to the absence of a PM effect among persons without prior heart disease who experienced a primary cardiac arrest. *Journal of Exposure Analysis and Environmental Epidemiology* (2001) 11, 86–96.

**Keywords:** air pollution epidemiology, ambient air pollution, local sources, measurement error model, particulate matter, personal exposure, topographic index.

## Introduction

In studies of air pollution and health effects, the ability to produce unbiased estimates of the pollutant exposure effect parameter is generally limited by the lack of available individual-level exposure data. Ideally, health effects (i.e., disease) models should be conditional on individuals’ true personal pollutant exposures. However, it is seldom feasible to measure personal exposures to air pollution.

Previously, we conducted a case–crossover study of out-of-hospital primary cardiac arrest in relation to daily particulate matter (PM) exposure in Seattle (Levy et al., 2001a). Analyses of daily average PM during the days immediately preceding primary cardiac arrest occurrence relative to reference days indicated no apparent associations. In this case–crossover study, the best available exposure data we had were surrogate exposures taken from

fixed-site ambient monitors. We conducted the exposure substudy described here to expand the ambient monitoring to three additional sites in an attempt to allow us to take into account topographic and atmospheric conditions in estimating personal exposure to ambient pollutants. These effects were then incorporated into a re-analysis of the case–crossover data.

Fine particulates are generally uniformly distributed over a region when any atmospheric agitation is present to disperse them. Previous research has shown a generally high correlation between airborne particle concentrations measured in various locations across the airshed in the Seattle metropolitan area (Larson et al., 1992). However, during periods of air stagnation, such as wintertime atmospheric inversions, heterogeneity in the spatial distribution of fine particulates can develop as a function of the distribution of PM pollution sources and surface features determining residual air flow. One of the important sources of fine PM air pollution in the Pacific Northwest is wood smoke. During colder periods in the winter, layered haze from wood smoke can be seen readily in some low-lying areas. Clear seasonal patterns in PM pollution that are determined, at least in part, by wood smoke production are evident (e.g.,

1. Address all correspondence to: Dr. Lianne Sheppard, PhD. Box 357232, Departments of Biostatistics and Environmental Health, University of Washington, Seattle, WA 98195-7232. Tel.: +1-206-616-2722. Fax: +1-206-616-2724. E-mail: sheppard@biostat.washington.edu  
Received 26 April 2000; accepted 21 August 2000.

Sheppard et al., 1999). An investigation during the wood-burning season of the average source contributions to airborne particulates in Seattle neighborhoods (Larson et al., 1989) indicated that during the day (7 a.m.–7 p.m.), wood burning contributed 54%, engine combustion 39%, marine sources 3%, and road dust 5%. At night time (7 p.m.–7 a.m.), when concentrations were greatest, wood burning contributed 82%, engine combustion contributed 17%, and other sources <1%.

During periods of stagnation, surface radiation inversions develop where cold air is trapped close to the ground and particulates from wood stoves and other emission sources accumulate. Using a mobile nephelometer (which measures fine PM in the range of 0.1–1.4  $\mu\text{m}$  in diameter), Larson et al. (1989) observed an inverse relation between elevation and particulate concentration under near stagnant atmospheric conditions. However, because of the influence of topography, the distribution of ambient fine particulates under stagnant conditions may be more aptly described in terms of “watershed” than simply in terms of elevation. Topographic contours may create bowls or basins at higher elevations where drainage can collect, making elevation an imperfect correlate of the disposition of wood smoke.

Because of the hilly topography and local variations in wood burning, we expected that systematic variation in the spatial distribution of ambient fine PM air pollution would alter personal exposure to ambient PM in the greater Seattle area. This could potentially bias health effects analyses. We hypothesized that we could adjust regional monitoring measures of PM exposure for subject-specific attributes by predicting personal exposure based on features ascribed to residence location. We hypothesized that the following properties would be important factors in personal exposure to ambient PM:

1. during high particulate pollution episodes and winter inversions, people living “downstream” will be exposed to more particulates than people nearer the top of the airshed;
2. areas with greater density of active fireplaces and wood stoves are likely to yield more PM than areas with lesser density; and
3. subjects are likely to be at home for a large proportion of a 24-h period, particularly at night when ambient PM concentrations peak.

Assumption (1) implies that residence location is an important factor in the level of PM exposure. More importantly for any study that relies on time-varying PM exposure, the magnitude of the residence effect may vary over time as a function of atmospheric conditions. Specifically, we are interested in time-varying interactions of location with temperature and atmospheric stagnation

because these have the potential to reorder exposures within person and change the case–crossover results. Assumption (2) is guided by studies where elevated indoor fine particulate levels have been found in suburban wood-burning neighborhoods, even in non-wood-burning houses (Anusewski et al., 1998). Non-urban locales generally exhibit more wood burning than urban locales, and urban/non-urban classification may be a reasonable initial proxy for wood-burning activity. Assumption (3) is essential for using residence location alone to adjust PM exposure for location. Ideally, we would have location-specific time–activity information for all cases on their case–crossover study index and referent days. Note that further assumptions would be necessary to adjust for inhaled dose rather than exposure.

The primary focus of this paper is to propose a method to adjust for residence location and atmospheric conditions in an air pollution health effects case–crossover analysis. We developed models for PM exposure based on geographic location and time-varying interactions with atmospheric conditions. We expanded the initial disease model from the original study (Levy et al., 2001a) to incorporate two additional models, an *exposure distribution* and a *measurement error* model. We assumed that only the disease model incorporates the exposure effect parameters of interest. Since personal exposure was not observed, it was necessary to substitute an estimate of it from a model. This estimate will only improve health effect parameter estimation to the degree that the data and model are rich enough to describe important sources of variation in the true personal exposures. Finally, we repeated the case–crossover analysis, adjusting for the exposure and measurement error modeling.

## Methods

### Data

The original study was a case–crossover study of the effects of PM air pollution on out-of-hospital primary cardiac arrest. We included 362 cases from a population-based case–control study (Siscovick et al., 1995). Cases were attended by paramedics in King County, Washington between October 3, 1988 through July, 25 1994. The subset enrolled was restricted to married King County residents aged 25–75 without clinically recognized heart disease or life-threatening comorbidities. Daily averages of regional PM monitoring data from nephelometry and gravimetric PM<sub>10</sub> were used as exposure measures. PM measures on index days, i.e., the day prior to the event for each case, were compared with PM measures from referent days, i.e., the same day of the week in the same month and year as the case event using conditional logistic regression. For further details of the study, see Levy et al. (2001a). Methods of

case–crossover analysis are described in Lumley and Levy (2000) and Levy et al. (2001b).

We used a measure of drainage flow as the topographic index (TI) for classifying airshed. Most physically based models of hydrologic and geomorphic processes rely on characterizations of local slope and the drainage area per unit contour length to portray the effect of topographic routing of runoff (Beven and Kirkby, 1979; O’Loughlin, 1986). TI is defined as  $\ln(a/\tan B)$ , where  $a$  is the upslope drainage area per unit contour length and  $B$  is the local ground slope. It reflects the spatial distribution of soil moisture, surface saturation, and runoff generation processes (Beven and Kirkby, 1979; Moore et al., 1986; O’Loughlin, 1986). High values of the TI correspond to downstream locations predicted to be wetter due to either a larger contributing area (and hence a greater supply of runoff) or a lower slope (and hence slower drainage of the supplied runoff). Because runoff is affected by surrounding topography, we hypothesized that the TI would serve as a better surrogate than elevation for the behavior of PM in the airshed under stagnant conditions.

For this exposure substudy, we obtained nephelometer data from three monitors from the Puget Sound Clean Air Agency (PSCAA) for a 1-year period (January 6, 1998–January 5, 1999) and averaged them to produce the regional PM measurement. This is identical to the procedure used to define fine PM from nephelometry during the original study period. Local PM data were collected from four monitors (one of these was also a regional monitor) during the same substudy time period. The local monitors were situated to represent one pairing of TI (up- versus downstream) and urban versus suburban location. Table 1 summarizes properties of these nephelometers. Beacon Hill and the nearby Rainier Valley locations were selected to represent contrasting TIs in an urban setting. Two Lake Forest Park (LFP) nephelometers provided a contrast of up- versus downstream sites in a suburban Seattle setting. The existing LFP Center nephelometer is situated at a downstream point at the bottom of a large hill in a suburban residential community. We placed another nephelometer at the LFP Reservoir on top of a ridge — an upstream site — 1 mile away. Both lie within a suburban residential community known for pervasive wood burning.

**Table 1.** Properties of air pollution monitoring sites.

Site	TI	Elevation (m)	Urban/suburban	Monitor designation
LFP Reservoir	-0.503	150	Suburban	Local
Beacon Hill	0.076	91	Urban	Local
Rainier Beach	1.989	35	Urban	Local
LFP Center	2.258	21	Suburban	Both
Kent	2.332	11	Suburban	Regional
Duwamish	7.596	4	Urban	Regional

In addition, we considered two time-dependent covariates: daily average temperature and measure of stagnation derived from hourly wind speed data. Temperature data were recorded at the Seattle–Tacoma International Airport and obtained from National Oceanic and Atmospheric Administration publications. Wind speed data were recorded at each of the three regional PM monitoring stations and obtained from PSCAA. The stagnation index is designed to depict the duration of calm conditions over a day that allow pollutant levels to build up rather than disperse (Norris et al., 2000). It is conceptually a better index of stagnation than the more common 24-h average wind speed. Hourly wind speed measurements were defined as stagnant if they were lower than the 25th percentile of all hourly measurements for that site over the substudy period. The number of stagnant hours in a day (with a minimum of 17 of 24 possible required) was tallied and then averaged across the three available sites.

The residence of each case in the case–crossover study and each of the nephelometers were geocoded, i.e., assigned values of latitude and longitude (Qualitative Marketing Software, 1997). The resulting coordinates were processed with geographic information systems (GIS) algorithms for calculating TI. Five of 362 cases were excluded because they only provided addresses outside King County. Cases and nephelometer sites were designated urban or suburban based on administrative boundaries.

#### *Descriptive and Exploratory Analyses*

We conducted a detailed exploratory regression analyses of the logarithm of local PM in the four locations on the logarithm of regional PM while examining a range of predictors. The predictors included regional PM, TI, urban/suburban designation, season, day of week, daily stagnation, daily temperature, and interactions with stagnation and/or temperature. We used the log scale because the models were simpler and this approach stabilized the variance. Modeling on this scale also assumes multiplicative effects and a multiplicative measurement error model.

We considered fixed location effects (TI and urban/suburban designation) and time-dependent interactions of these effects. We were particularly interested in potential time-dependent interactions because these have the potential to reorder exposures on the case and referent days in the disease model. Variables with this potential are temperature and stagnation index. If the measurement sites show different PM levels as a function of stagnation or temperature, then this implies that individual exposures are not well represented by the regional PM measurement used in our primary analysis on some days. For instance, an interaction of stagnation with TI would mean that adjustments to the ambient PM measurement would vary over time and as a function of location. This adjustment would alter the relative magnitude of the PM level across strata

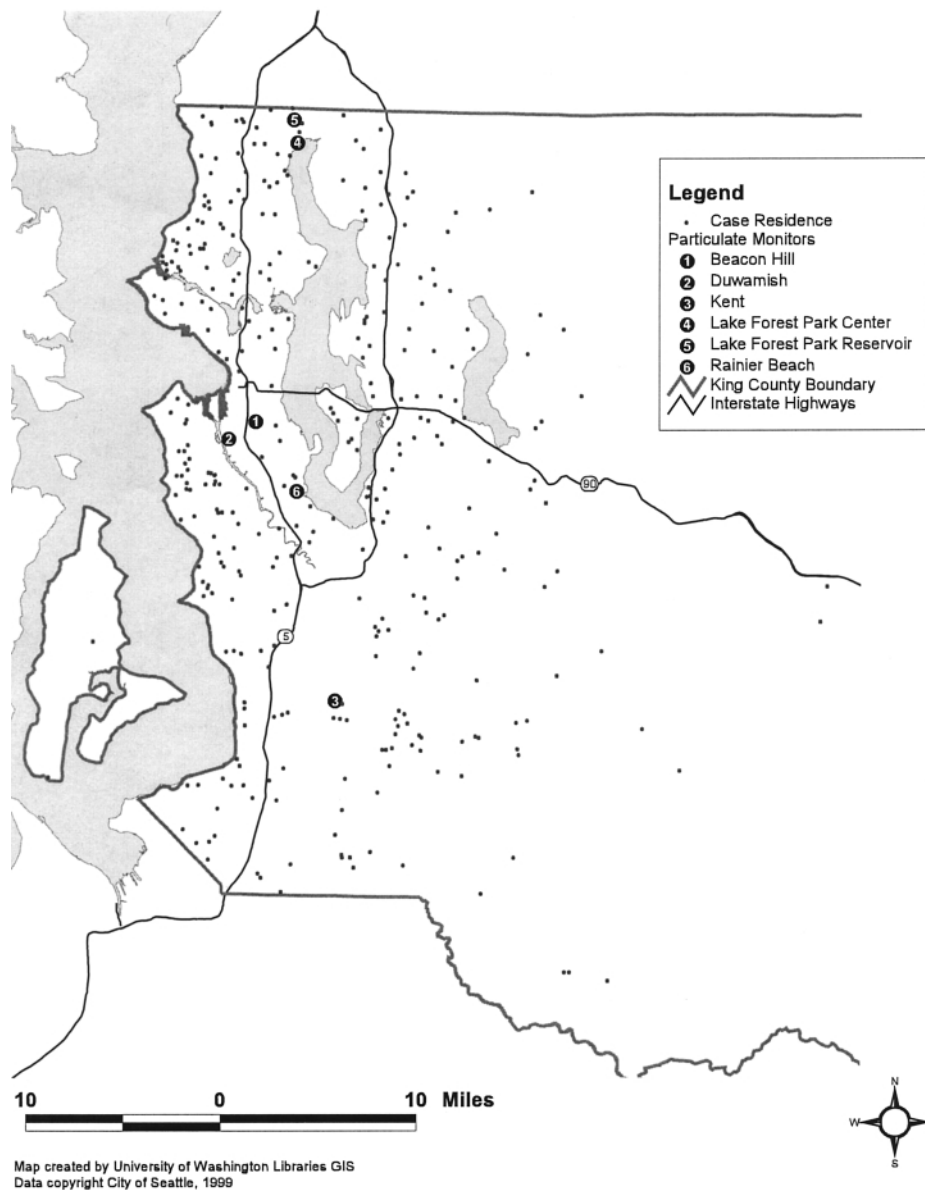
and, more importantly, reorder the cases' index and referent day exposures within strata.

Model selection was done without consideration of the dependence in the data. Once the models were selected, final models were fit with a spatial exchangeable dependence structure.

*Personal Exposure Modeling and Predictions*

Exposure modeling posed significant challenges because the true exposure and its distribution were not observed. Our interest was in the ambient source personal exposure. This differs from total personal exposure. We hypothesized that

true personal exposure to person  $s$  on day  $t$  could be partitioned into ambient source ( $X_{st}$ ) and non-ambient source ( $I_{st}$ ) components:  $X_{st} + I_{st}$ . We assumed that a person's residence location would represent his/her ambient source pollution exposure, i.e., that people do not move around in space. Then  $s$  will also index spatial location. We further assume that people are fully exposed to ambient air so there is no decrease in their personal ambient source exposure due to pollutant penetration or deposition. These latter two assumptions may not be justified, but given we lacked data to address them directly, they were useful for this modeling exercise. Research by Mage et al. (1999)



**Figure 1.** Map of the greater Seattle map of the greater Seattle area with monitoring sites and subject residences.

suggests that ambient source and non-ambient source components are independent over time; therefore, ignoring non-ambient sources in short-term health effects studies relying on ambient monitoring data is unlikely to cause bias. Given these assumptions, we developed a model for true personal ambient source exposure,  $X_{st}$ , conditional on ambient monitor measurements of light scattering,  $W_{st}$ , at spatial location  $s$  and time  $t$ .

We assumed a multiplicative model for ambient pollution over time and space. We assumed that both  $W$  and  $X$  were lognormally distributed. On the log scale, these variables are jointly normal. The model is additive and will be composed of a linear function of covariates along with a variance term. As will be shown in the *Results* section, the covariates included same-day regional ambient measurements, a site-specific indicator, an indicator for winter season, air stagnation index, average daily temperature, and interaction terms for stagnation on hilltop sites and temperature at suburban wood-smoke-exposed valley sites. We allowed for constant correlation between measurements on the same day at different locations (regardless of distance), and no correlation at different times, whether at the same or a different site. The variance model was based on extensive analysis of PM monitoring measurements in the greater Seattle area (unpublished data available from the first author). In order to correct the disease model, we predicted the location- and time-specific personal exposure measurements conditional on ambient measurements, written  $E(X|W)$ . [Further description of this approach to modeling (using slightly different exposure and measurement models and applied in a Poisson regression context) can be found in Sheppard and Damian, 2000.] To estimate  $E(X_{st}|W_{st})$ , we applied the model developed from the exposure substudy on a case-specific basis to the regional PM and other measurements from subjects' index and referent days in the case-crossover study. Since the locations represented in the substudy were much more limited than the case residences, arbitrary cut-offs based on substudy data were necessary. Rationalizations for the specific cut-offs chosen are given in the *Results* section.

#### Corrected Disease Model Estimates

Under no exposure measurement error, air pollution case-crossover studies can be analyzed using conditional logistic regression under appropriate stratification (Lumley and Levy, 2000). With exposure measurement error, quasi-likelihood estimating equations can be used to estimate the disease model parameters while treating the exposure and measurement model parameters  $\tau$  as nuisance parameters. Liang and Liu (1991) show how a model for  $X|W$  can be applied in case-control applications analyzed by logistic regression. They substitute  $E(X|W)$  for  $X$  in a standard (matched) case-control analysis under a normal distribution assumption for the measurement error and exposure

distributions. This still produces a biased estimate,  $\beta_{JS}$ , of the "true" exposure effect parameter  $\beta$ , but this bias is much smaller than for the estimate obtained by ignoring the measurement error, i.e., in the model using the ambient data directly. Furthermore, the test of  $\beta_{JS}=0$  is valid and consistent estimates of  $\beta$  are possible by scaling the estimated  $\beta_{JS}$ . Further methodologic work is needed to accommodate measurement error under lognormal measurement error and exposure distribution assumptions; for this paper, we will use the results of Liang and Liu (1991) without alteration.

## Results

### Descriptive and Exploratory Analyses

Table 1 gives a list of all six monitoring sites used in this study and Figure 1 shows their geographic location. The first four monitors are the four local monitors used in the exposure substudy. The last three monitors are regional monitors that provided data for both this substudy and the original case-crossover study. Note that the LFP Center monitor functions as both a regional and a local monitor. *A priori*, it was expected that this local monitor would not exhibit any location effect in our models with regional PM as a predictor. Although this property does not hold in general, for these six monitors, the TI and elevation measures give the same rank ordering.

Table 2 gives the distribution of the time-varying variables used in the exposure substudy. The local PM measurements tend to be lower than the regional summary. As expected, regional PM is most similar to the LFP Center local monitor since it also contributes to the regional PM measurement. All the PM measurements show evidence of positive skewness. Note that 90% of the days in the study year has 11 or fewer stagnant hours. Furthermore, temperature extremes are rare — only 9 and 2 days in the

**Table 2.** Distribution of time-varying variables.

Variable	10%	25%	50%	75%	90%	Mean
LFP Reservoir PM ( $b_{sp}$ )	0.08	0.12	0.19	0.28	0.37	0.22
Beacon Hill PM ( $b_{sp}$ )	0.12	0.15	0.23	0.35	0.47	0.28
Rainier Beach PM ( $b_{sp}$ )	0.09	0.13	0.19	0.29	0.41	0.23
LFP Center PM ( $b_{sp}$ )	0.15	0.20	0.29	0.42	0.58	0.36
Regional PM ( $b_{sp}$ )	0.17	0.23	0.32	0.46	0.58	0.38
Stagnation (h)	1	2	6	8	11	6
Average temperature (°F)	42	46	52	62	67	53

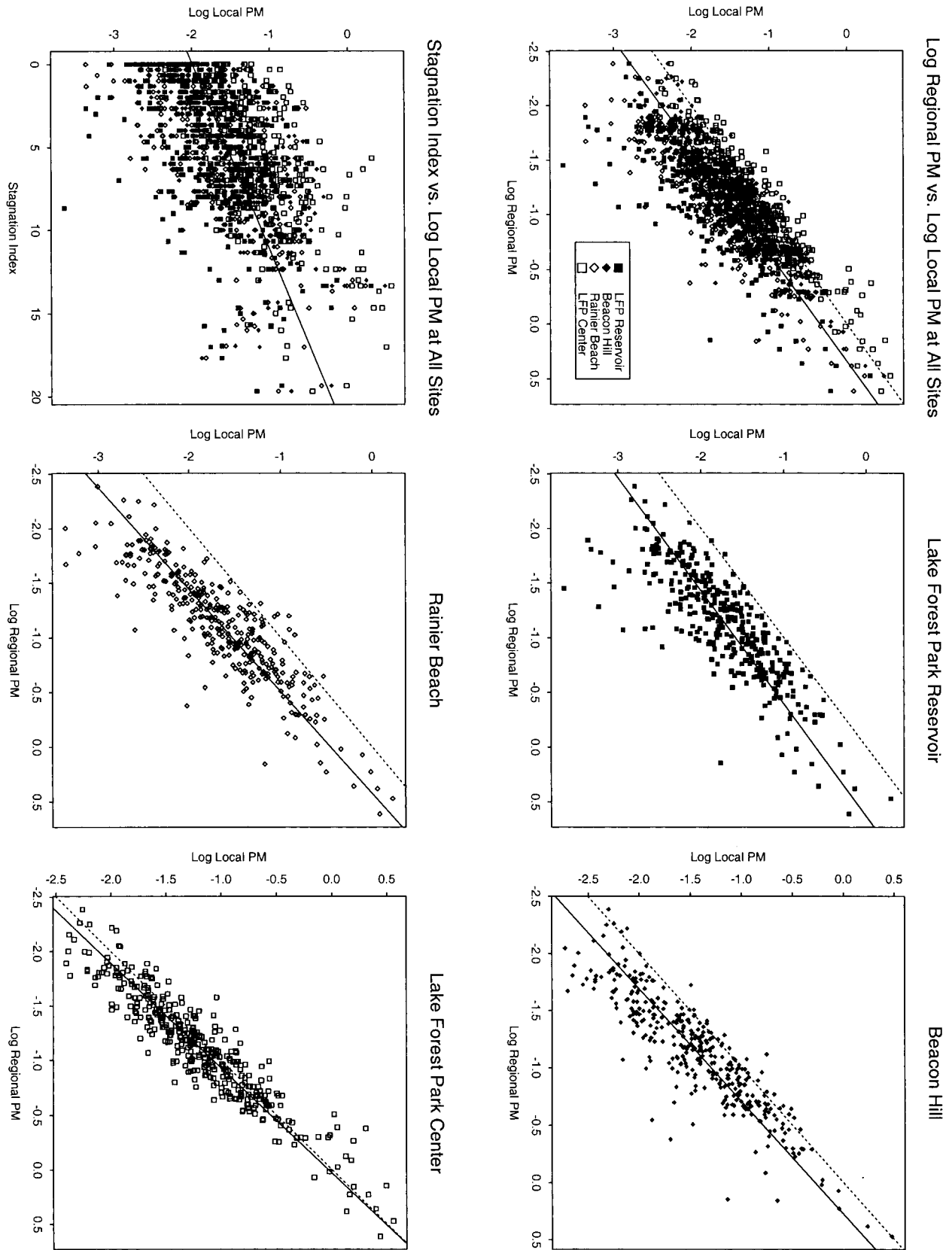


Figure 2. Scatterplots of the regional versus local PM data.

**Table 3.** Analysis of deviance table.

Number	Model terms	df	Deviance	df change	Deviance change
1	Regional PM	1422	163.5		
2	1+site indicator+ winter season	1418	99.8	4	63.7
3	2+stagnation+ temperature	1416	99.6	2	0.2
4	3+LFP Reservoir stagnation+ LFP Center temperature	1414	91.9	2	7.7
5	2+stagnation+LFP Reservoir stagnation	1416	97.0		
6	2+temperature+LFP Center temperature	1416	94.6		
7	2+LFP Reservoir stagnation+ LFP Center temperature	1416	92.5		

study period had average temperatures below 32 or above 75°F, respectively.

Figure 2 shows regional PM *versus* local PM on the log scale at each local site. On each site-specific plot is a best-fitting regression line displayed as the solid line as well as the dashed  $x=y$  line. The strong association between PM measures is consistent across location. The most obvious difference between locations is in the average level (regression intercept — contrast the solid regression line to the dashed  $x=y$  line), indicating a multiplicative difference in PM levels on the original (or native) scale. However, in our four sites, the location factors alone or in combination did not give a good summary of these differences. The pattern was not consistent with either the TI (filled symbols=upstream) or urban/suburban (square symbols=suburban) dichotomies. With only four sites, we had inadequate information to simplify the model with respect to these location variables. Therefore, we included site-specific intercepts in the model instead of the urban/suburban designation and/or the TI linear term.

Also shown in Figure 2 is the relation between stagnation index and log local PM. This association, while not as compelling as the regional PM association, is also quite strong. We also examined temperature *versus* local PM (not shown). There was no consistent association with temperature. Further exploration of other variables led us to rule out day of week effects and add a winter season adjustment.

In exploratory models of interactions with stagnation and temperature, we detected one site-specific interaction for each variable. We found that the stagnation effect was positive (with increasing stagnation) for all sites except LFP Reservoir which showed a negative association with increasing stagnation. This site had the lowest TI ( $-0.503$ ) and highest elevation at 150 m on the top of a hill. We found an effect of temperature at the LFP Center location that was positive with decreasing temperature. This site has the highest TI and lowest elevation of all the local sites.

Table 3 gives an analysis of deviance table for a series of seven models. In comparison to the model with regional PM alone, the site and winter season indicators allowed a substantial reduction in the deviance. Main effects for stagnation and temperature did not improve the model fit, but inclusion of the site-specific interactions for these variables (called LFP Reservoir stagnation and LFP Center temperature) yielded another significant drop in the deviance. Among models with either both stagnation terms or both temperature terms (models 5 and 6), the temperature model gave the best fit. For most purposes, we selected model 4 as our final model which included main effects and interactions for both temperature and stagnation. Estimates from this model are given in Table 4. As discussed in the *Methods* section, we developed the variance model by assuming that measurements were independent over time and had constant correlation across sites within

**Table 4.** Coefficient estimates and standard errors for the final model.

Parameter	Estimate	Standard error	<i>z</i> -statistic
<i>Fixed effect coefficients</i>			
Intercept	-0.385	0.036	-8.3
Regional PM	1.035	0.024	43.0
Beacon Hill site	0.143	0.026	5.5
Rainier Beach site	-0.092	0.026	-3.5
LFP Center site	0.385	0.026	14.8
Winter season	-0.185	0.025	-6.3
Stagnation	0.003	0.003	0.9
Temperature	0.002	0.001	2.2
LFP Reservoir stagnation	-0.025	0.003	-7.1
LFP Center temperature	-0.013	0.001	-9.9
<i>Variance parameters</i>			
$\sigma^2$ between sites	0.014	0.002	6.7
$\sigma^2$ error	0.051	0.002	23.0

days. The within-day residual correlation from this model (after adjusting for all the predictors) was 0.22.

*Predicted Exposures*

Table 5 gives the distribution of variables used in the exposure prediction. For time-varying variables, we only included index and referent days in the 1988–1994 case accession period. Note that a reasonable fraction of the cases (22%) lives at locations with larger TIs than the LFP Center monitor, the substudy monitor with the largest TI. For time-varying predictors, the stagnation distribution was similar to the 1998–1999 exposure substudy period, while the average temperature was approximately 2°F lower. Regional PM was notably higher than the measurements from the substudy. Some of these differences will be due to the greater proportion of sudden cardiac arrests during the higher PM winter season. For the PM measurements, another cause of this difference is the overall downward trend in PM levels in the greater Seattle area over the past 15 years (see, e.g., Fig. 1 in Levy et al., 2001b). Regardless of the cause, it is important to note that application of the model developed from the exposure substudy to the case–crossover data involves extrapolation to a different time period.

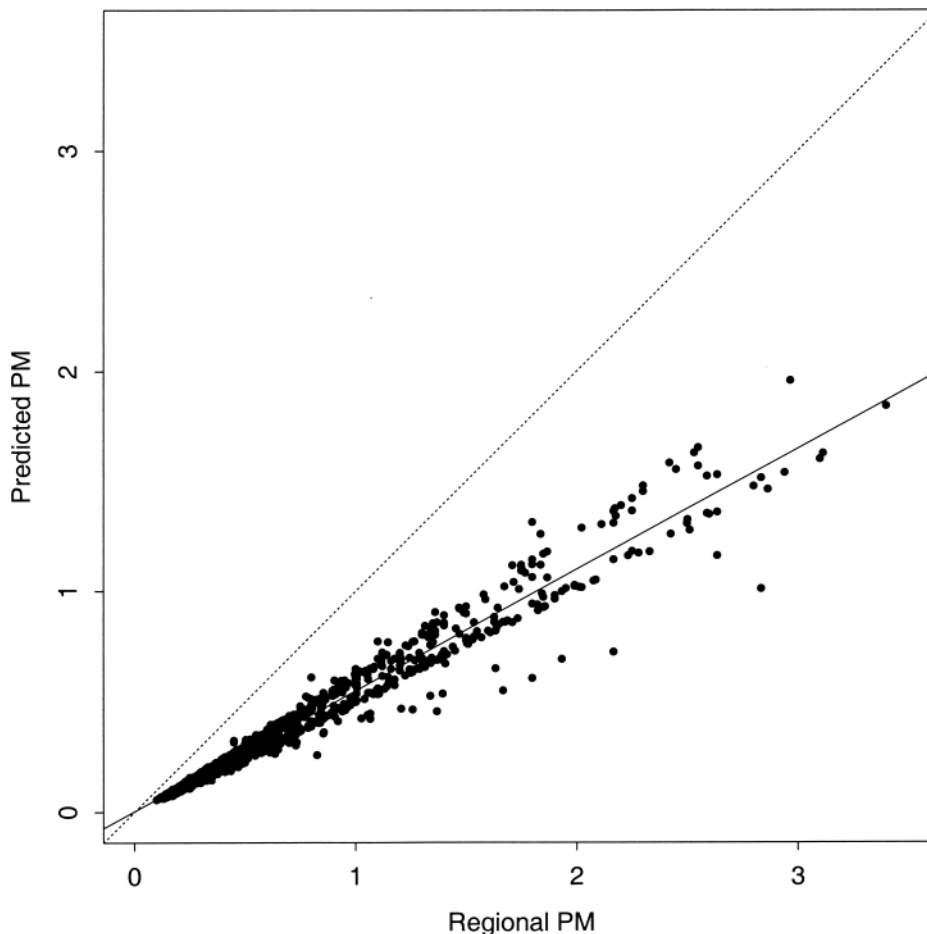
To predict subject-specific exposures, we applied the model developed from the exposure substudy on a case-specific basis to the regional PM and other measurements from subjects' index and referent days in the case–crossover study. We could apply the model directly to all predictors except the site intercepts. Since we did not find a pattern to the intercepts that allowed us to develop a simple model, we have no basis for determining the relative PM level at any subject's residence. Thus, any choice would be arbitrary. We assumed that the average PM level for each subject was equivalent to the Beacon Hill site average because this site was closest to the grand mean. We also had to select category boundaries to apply to individual subjects for the location-specific time-dependent predictors. Again, given the limitations in our data, these choices are arbitrary. For the stagnation interaction, we included all subjects with a TI less than –0.5. This selected subjects living at the highest elevation and most upstream sites, sites that were at least as extreme as the LFP Reservoir site. The temperature interaction was more challenging since the results suggested that factors other than LFP Center's low-elevation, downstream location were important. High wood smoke levels may have contributed to the interaction, but we had no adequate measure of wood stove density to verify this

**Table 5.** Distribution of variables for exposure predictions in the case–crossover analysis.

TIs across subjects						
Variable	10%	25%	50%	75%	90%	Mean
TI	–0.22	0.42	1.09	2.07	3.46	1.48
Cases by location predictor classification						
TI	Urban		Suburban		All	
Upstream (< –0.5)	5		11		16	
Neutral	82		182		264	
Downstream (> 2.25)	14		63		77	
All	101		256		357	
Time-varying predictors and predictions — values on index and referent days						
Variable	10%	25%	50%	75%	90%	Mean
<i>Predictors</i>						
Regional PM ( $b_{sp}$ )	0.23	0.31	0.50	0.86	1.40	0.68
Stagnation (h)	1	2	5	9	13	6
Average temperature (°F)	39	44	50	59	65	51
<i>Predictions<sup>a</sup></i>						
Model 4 prediction ( $b_{sp}$ )	0.12	0.17	0.28	0.47	0.77	0.37
Model 5 prediction ( $b_{sp}$ )	0.12	0.17	0.28	0.48	0.78	0.38
Model 6 prediction ( $b_{sp}$ )	0.16	0.21	0.35	0.61	0.96	0.47

<sup>a</sup>Given the limitations of the exposure model, predictions are only valid up to a scale factor.





**Figure 2.** Regional PM *versus* predicted PM using the final model (model 4).

speculation. Lacking these specific data, we applied the interaction term to all subjects who lived in suburban high TI locations ( $TI > 2.25$ , more extreme than the LFP Center location). As sensitivity analyses, we also developed predictions based on alternative models with only one of the time-dependent interaction terms.

Predictions for the subject-specific index and referent days are summarized in Table 5 for models 4, 5, and 6 from Table 4. Note that the predictions tend to be much lower than the regional PM values used in the original

analysis and the spread is less. This could be, in part, a scaling problem. Figure 3 shows the predictions from model 4 *versus* the regional PM values. The estimates tend to follow three rays: two for the winter *versus* non-winter days, the last for the additional reduction in PM on high stagnation days for subjects living in upstream locations. The deviation of the slope from 1 is due to the scaling of the data. This cannot be adequately resolved with only four sites and site-specific intercepts in our exposure model.

**Table 6.** Case-crossover analysis results for an interquartile range (IQR) change in  $b_{sp}$  (0.5).

Predictor	Relative risk estimate <sup>a</sup>	95% CI <sup>a</sup>	Wald $\chi^2$	<i>p</i> -value
Regional PM	0.90	(0.78, 1.04)	2.34	0.13
Model 4 prediction	0.90 <sub>c</sub>	(0.80, 1.02) <sub>c</sub>	3.00	0.08
Model 5 prediction	0.91 <sub>c</sub>	(0.81, 1.02) <sub>c</sub>	2.71	0.10
Model 6 prediction	0.92 <sub>c</sub>	(0.83, 1.02) <sub>c</sub>	2.63	0.11

<sup>a</sup>Given the limitations of the exposure model, the estimates and standard errors are only valid up to a scale factor of  $c$  where  $0 < c < \infty$ . Estimates reported are scaled to make the model 4 prediction RR estimate equal to the regional PM RR estimate.

### Case–Crossover Study Results

Table 6 gives the effect estimates for the associations of PM with primary cardiac arrest for the case–crossover study. First is the original result for regional PM lagged 1 day, slightly different because we dropped the five cases without King County addresses in this analysis. The remaining estimates from the prediction models are also negative. We emphasize that we did not have enough information to scale the predictions properly. This directly affects the health effect estimates. We do note that the predictions produce effect estimates that are also negative and more nearly statistically significant than the estimate using regional PM. Under the assumptions that the exposure and measurement models are correct and that a lognormal model prediction will behave similarly to a normal prediction in this disease model, the tests given in Table 6 are valid for the hypothesis that  $\beta=0$  (Liang and Liu, 1991).

### Discussion

The exposure analysis alone gives evidence that daily ambient air pollution exposures in King County vary by residence location and location-specific time-varying functions of temperature and stagnation. While initially surprising, our results are consistent with the combined effects of the physics of surface radiation inversions and seasonal wood burning. During these inversions, the air next to the surface is denser than the air above the surface. In hilly terrain, this denser surface air at the hilltop flows downhill and is replaced at the hilltop surface by air from above. This latter air has not swept past surface pollution sources, whereas the dense air flowing downhill accumulates pollution along its path, most notably wood combustion byproducts. The result is clean hilltops and polluted valleys, as particle-laden air pools in low-level locations. The LFP area is known for wood burning and high levels of wood smoke. The net effect of the inversions coupled with local wood smoke sources is to make the LFP Reservoir site cleaner than expected and the LFP Center site more polluted. It is notable that the temperature effect is apparent even though the LFP Center site is one of the three regional sites and the regional sites are all low-elevation, downstream sites. It is unlikely, therefore, that the interaction is determined completely by elevation or TI. We believe that the distinction in this location is due to more cold-weather-induced wood burning than in the industrial Duwamish or mixed residential and light industrial Kent areas.

Our goal of the exposure analysis was to make residence-specific predictions of ambient PM levels. For the predictions to be valid, we are assuming that the exposure model is correct and that predictions developed from air pollutant and atmospheric measurements made in

1998–1999 are valid for the 1988–1994 time period of the case–crossover study. Since our model did not have parametric terms for TI, we needed to apply an arbitrary TI adjustment to all subjects. This will not affect the significance of results in a case–crossover study since all comparisons are within subjects, but it does mean that the scaling of the relative risk parameter estimate is arbitrary. More importantly, with only four sites, we do not have enough information to determine whether it is elevation, TI, the suburban location, or some function of all of these that makes the LFP sites perform differently than the other sites as a function of stagnation and temperature. We also do not have enough information to categorize accurately residences whose exposures are influenced by the time-dependent interactions. We consequently selected arbitrary category boundaries that are based on our understanding of the underlying processes at work. We must recognize that other choices will be equally well supported by these data, yet may result in different predictions and case–crossover study results.

In this paper, we have also outlined an approach to incorporating residence-specific adjustments to ambient monitor measurements into a health effects analysis. This approach has the potential to alter original study findings even though in this application we obtained adjusted health effect estimates generally consistent with the original analysis. The lack of change in these results may be due either to limitations of the exposure substudy itself or to an underlying lack of effect of PM on primary cardiac arrest in people without prior clinical heart disease, as reflected in the null results of the original analysis.

The methodologic approach we outlined deserves additional evaluation in a setting with a more substantial exposure substudy and where health effects are more likely. Our substudy included only four local sites. This lack of spatial resolution severely limited the generalizability of the exposure model we developed. While it is surprising that this study had fine-enough spatial resolution to describe several sources of time-dependent variation that meaningfully modify ambient air pollution levels, the spatial resolution is clearly insufficient for making residence-based ambient PM exposure predictions. We also made other simplifying assumptions due to lack of data. Most notably, we assumed that a person's residence location represents his/her daily ambient exposure, and that location-adjusted ambient levels represent total personal exposure to ambient PM. Research currently in progress will allow us to improve the exposure model using personal exposure measurements obtained from a series of panels of individuals, as well as use a more promising health effects analysis from a case series of more susceptible population of cardiac arrest cases among people with prior heart disease. The question of whether it is necessary to adjust ambient PM exposure measurements for personal characteristics in health effect

studies conducted in topographically diverse cities such as Seattle remains unanswered.

### Acknowledgments

We thank David Montgomery and Harvey Greenberg from the Department of Geology at the University of Washington for their assistance with the TI calculations. We also thank Timothy Larson from the Department of Civil Engineering at the University of Washington for helpful discussions on the physics of inversions. This research was funded, in part, by contract no. 97-2-2 from the Health Effects Institute and grant ES08062-03 from the National Institute of Environmental Health Sciences, NIH. The contents are solely the responsibility of the authors and do not necessarily represent the official views of HEI or NIEHS.

### References

- Anusewski J., et al. Simultaneous indoor and outdoor particle light scattering measurements at nine homes using a portable nephelometer. *J. Expos. Anal. Environ. Epidemiol.* 1998; 8: 483–493.
- Beven K., and Kirkby M.J. A physically based, variable contributing area of basin hydrology. *Hydrol. Sci. Bull.* 1979; 24: 43–69.
- Larson T., et al. Urban air toxics mitigation study, phase 1. Technical Report, Puget Sound Air Pollution Control Agency, Seattle, Washington, 1989.
- Larson T., et al. Weekly composite sampling of PM<sub>2.5</sub> for total mass and trace elements analysis. In: Chow J. (Ed.), Transactions of the Specialty Conference on PM<sub>10</sub> Standards and Non-Traditional Particle Source Controls. Air and Waste Management Association, Pittsburgh, PA, 1992, pp. 39–50.
- Levy D., Sheppard L., Checkoway H., Kaufman J., Lumley T., Koenig J., and Siscovick D. A case–crossover analysis of fine particulate matter air pollution and out-of-hospital sudden cardiac arrest. *Epidemiology* 2001a: 12 (in press).
- Levy D., Lumley T., Sheppard L., Kaufman J., and Checkoway H. Referent selection in case–crossover analyses of acute health effects of air pollution. *Epidemiology* 2001b: 12 (in press).
- Liang K.Y., and Liu X.H. Estimating equations in generalized linear models with measurement error, Chap. 4. In: Godambe V.P. (Ed.), Estimating Functions. Oxford University Press, Oxford, 1991, pp. 47–63.
- Lumley T., and Levy D. Bias in the case–crossover design: implications for studies of air pollution. *Environmetrics* 2000: 11: 689–704.
- Mage D.T., et al. Assessment of human exposure to ambient particulate matter. *J. Air Waste Manage. Assoc.* 1999; 49: 1280–1291.
- Moore I.D., et al. Hydrologic characteristics and modeling of a small, forested catchment in southeastern New South Wales: prelogging condition. *J. Hydrol.* 1986; 83: 307–335.
- Norris G., Larson T., Koenig J., Claiborn C., Sheppard L., and Finn D. Asthma aggravation, combustion, and stagnant air. *Thorax* 2000; 55: 466–470.
- O’Loughlin E.M. Prediction of surface saturation zones in natural catchments by topographic analysis. *Water Resour. Res.* 1986; 22: 794–804.
- Stardata. Qualitative Marketing Software, Inc., Dallas, Texas, 1997.
- Sheppard L., and Damian D. *Environmetrics* 2000: 11: 675–687.
- Sheppard L., Levy D., Norris G., Larson T., and Koenig J. Effects of ambient air pollution on non-elderly asthma hospital admissions in Seattle, Washington, 1987–1994. *Epidemiology* 1999; 10: 23–30.
- Siscovick D.S., Raghunathan T.E., King I., Weinmann S., Wicklund K.G., Albright J., Bovbjerg V., Arbogast P., Smith H., Kushi L.H., et al. Dietary intake and cell membrane levels of long-chain *n*–3 polyunsaturated fatty acids and the risk of primary cardiac arrest. *JAMA* 1995; 274: 1363–1367.



Copyright of Journal of Exposure Analysis & Environmental Epidemiology is the property of Nature Publishing Group and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.