Spatiotemporal Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort

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Project Duration: 36 Months

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ABSTRACT

Problem: Studies using the American Cancer Society (ACS) cohort to assess the relation between particulate air pollution and mortality rank among the most influential and widely cited. The original study, a reanalysis that introduced new random effects methods and spatial analytic techniques, and recent studies with longer follow-up and improved exposure assignment have all demonstrated statistically significant and substantively large air pollution effects on all-cause and cause-specific mortality. Due to this robust association and a lack of other studies on the long-term effects, the ACS studies have proven important to government regulatory interventions and health burden assessments.

California currently has no statewide studies assessing mortality resulting from air pollution in the general population. Existing estimates come from either national-level ACS studies where the California subjects comprised less than 10% of the total sample or from southern California, where questions about applicability to the rest of the State remain. Adopting either of these estimates can change the burden of illness attributable to air pollution by two to three fold. In addition, neither of the existing ACS studies have used high-resolution exposure assignment or investigated the temporal dimensions of the dose-response relationship.

Previous Work: Our previous work includes the original American Cancer Society study of particulate air pollution and mortality, the reanalysis of this study and the Harvard Six Cities study, many analytic extensions to these studies, and the first assessment of particulate air pollution at the within city or "intraurban" scale. In this last study our team documented the first assessment of mortality and particulate air pollution estimates for the intraurban or within-city scale in Los Angeles. Our results suggest the chronic health effects associated with intraurban gradients in exposure to $PM_{2.5}$ are even larger than previously reported across metropolitan areas. We observed effects nearly three times greater than in models relying on between-community exposure contrasts. Given these remarkable findings, a need exists to investigate whether the results hold for other parts of California or are sensitive to alternative measures of exposure assessment and confounding control. We have also been investigating whether there are temporal patterns in the relative risk of mortality from air pollution. These studies suggest that with increasing mobile source contributions there are increased dose-response functions over time, and these findings need further investigation to inform the science of health effects assessment and policy of air pollution control.

Objectives: We will pursue the following research objectives to reduce critical scientific uncertainties that impede effective policy action on air pollution: (1) To derive detailed assessments of the health effects from particulate and gaseous air pollution on all-cause and cause-specific mortality in California based on the American Cancer Society Cohort; (2) to investigate whether specific particle characteristics associate with larger health effects through examination of intraurban gradients in exposure to different particle

constituents and sources; and (3) to determine whether critical exposure time windows exist in the relationship between air pollution and mortality in California.

Description: We have identified 95,112 subjects in the ACS cohort who will serve as the study population (26,183 deaths with an 18 year follow up ending in 2000). These subjects are widely distributed across California, giving comprehensive coverage for much of the population of the State. For the first time in the ACS studies, we will geocode subjects to their home address. Previous studies have been restricted to zip code areas, limiting our ability to assign exposures based on proximity to source or on measures of traffic and potentially introducing non-differential measurement error.

As a basis for exposure assessment, we will utilize estimates derived by Air Resources Board staff for the California Teachers Cohort Study (led by Dr. Michael Lipsett, with Dr. Jerrett at co-I). We will also extend these estimates with advanced Bayesian Maximum Entropy kriging models to allow for spatiotemporal exposure assignment with explicit incorporation for errors in the exposure estimates. Following our recent national analysis, we will use these refined exposure data to assess whether critical exposure windows exist in the temporal mortality experience. We will also have the opportunity to assess risks from proximity to sources such as the Port of Los Angeles and the major highways in the State.

We will employ a comprehensive set of 44 individual confounders documented in earlier ACS studies investigating air pollution health effects. These variables control for lifestyle, dietary, demographic, occupational, and educational influences that may confound the air pollution-mortality association. We will also use ecological variables for the ZCAs to control for "contextual" neighborhood confounding (e.g., unemployment). Although we will utilize the variables used in previous analyses for promoting comparison to earlier results, we will also optimize the model for individual risk factors of the California population as a sensitivity analysis.

Benefits: California has no state-wide estimates of mortality to support policymaking and regulatory activities. Extension of the ACS study to address scientific uncertainties and to derive estimates specific to California will assist the Air Resources Board and others to assess the benefits of policy interventions. We will also increase our understanding of specific source contributions to the mortality experience and of whether there are temporal patterns in the relative risks of mortality from air pollution. This information will strengthen the efforts of the ARB to implement policies that protect public health.

SIGNIFICANCE

In a recent analysis commissioned by the US Environmental Protection Agency seeking an expert consensus on risk of mortality from exposure to $PM_{2.5}$ (Industrial Economics Incorporated 2006), studies based on the American Cancer Society (ACS) Cohort were cited as influential by every expert panel member. The most recent study by Jerrett et al. [1], the first to examine the risks with improved exposure models based on intraurban gradients across Los Angeles, was continuously noted as one of the most important determinants of the risk from PM by the majority of the experts. The consistent results of higher risk estimates from this Los Angeles study, probably resulting from reduced exposure measurement error, have raised questions about which risk estimate should be used for assessing the benefits of air quality regulations in California. The California population of the Pope et al. [2] comprises less than 10% of the total study population (about 42,000 of 500,000 subjects). While the Jerrett et al. [1] study is based solely on California residents, questions about the applicability of the results for the remainder of California persist, given the generally higher levels of pollution in the Los Angeles region and the different population mixture there. ***This study will derive the first California-wide estimates of mortality associated with $PM_{2.5}$ exposure and other criteria co-pollutants, thus supplying policymakers with a valuable resource for deriving benefits estimates.***

Beyond the immediate contributions to benefits estimation, this study will also resolve key uncertainties in the science of air pollution health effects. For the first time we will geocode the ACS subjects to their home address, as compared to the previous studies that have used either metropolitan area of residence or the home zip code to assign exposure. This improved locational accuracy will be combined with the most advanced geostatistical models of exposure and with direct measurements of proximity to sources such as freeways and ports. The combination of increased locational accuracy and reduced exposure measurement error may produce even larger estimates of risk than reported in previous studies, if the general pattern of heightened effects from better exposure assessment holds. We will also have capacity to test source specific effects through proximity assignment and through use of speciated particulate data.

The integration of numerous land use, traffic, physiographic, and remotely sensed data into a rigorous mathematical model capable of estimating exposures in time and space will extend the science of exposure assessment. In so doing, this research will develop a unique resource for future air pollution studies in California. For example, the results of these exposure assessments could be immediately applied to the California Teachers Cohort.

This study will also examine the question of whether critical exposure windows exist in the dose-response to pollution. Studies undertaken by our team as part of a nearly completed Health Effects Institute contract indicate that the health response for a given unit change in PM has probably increased over time in the national-level cohort [3]. In other words, although ambient levels have declined the dose-response curve appears to have become steeper in later follow up periods. There are many possible explanations for this finding such as heightened susceptibility in the cohort due to aging. Another possibility is that the continued focus on $PM_{2.5}$ mass reductions, without regard to the characteristics of PM, may have the effect of increasing the toxicity of the PM mixture, thereby resulting in the increased dose response and general lack of population health benefits. Greater understanding of how the dose-response changes over time will supply important information to the policy process about the timing of regulatory interventions.

BACKGROUND AND RATIONALE

American Cancer Society Study of Particulate Air Pollution and Mortality

Epidemiologic studies conducted over several decades have provided evidence suggesting that long-term exposure to elevated ambient levels of particulate air pollution is associated with increased mortality. Two U.S. cohort studies, the Harvard Six Cities Study [4], a 20 year prospective cohort study, and the American Cancer Society (ACS) Study [5] – a larger retrospective cohort study involving 156 cities – estimated that annual average all-cause mortality increased in association with an increase in ambient fine particle concentration ($PM_{2.5}$ - particles with an aerodynamic diameter less than 2.5 μm).

Both studies came under intense scrutiny in 1997 when the results were used by the EPA to support new National Ambient Air Quality Standards for $PM_{2.5}$ and to maintain the standards for particles with an aerodynamic diameter (PM10), already in effect. The findings were the subject of debate for the following reasons: possible residual confounding by individual risk factors (e.g., sedentary lifestyle, active or passive cigarette smoke exposure) or ecologic risk factors (e.g., aspects of climate or social milieu); inadequate characterization of the long–term exposure of study subjects; different kinds of bias in allocating exposure to separate cities; and robustness of the results to changes in the specification of statistical models [6, 7]. To address growing public controversy concerning the studies' methods and their results, Harvard University and the ACS requested that the Health Effects Institute [8] organize an independent reanalysis of these studies.

Overall, the Reanalysis assured the quality of the original data and replicated the original results. It tested those results against alternative risk models of the Cox proportional-hazards family and other analytic approaches. The various sensitivity analyses did not substantively alter the original findings of an association between indicators of particulate matter air pollution and mortality [9]. Phase II of the reanalysis made innovative contributions to the understanding of the air pollution-mortality association by developing new methods of spatial analysis for cohort studies involving both individual and ecologic covariates [10]. Key findings from the Reanalysis indicated that (1) educational status has a significant modifying effect with risk of mortality associated with fine particles declining with increasing educational attainment, (2) sulfur dioxide may exert a more robust effect on mortality than sulfates, (3) other possible ecologic confounders have no significant effect in models that control for spatial autocorrelation, and (4) spatial risk models attenuate the air pollution effect, both in terms of size and certainty.

Post-Reanalysis Studies of the ACS cohort

Following the Reanalysis, Pope and colleagues [2] undertook an analysis using an additional 10 years of data which doubled the follow-up time to more than 16 years and tripled the number of deaths. Exposure data were expanded to include gaseous co-pollutant data and new $PM_{2.5}$ data which had been collected since the enactment of the new air quality standards. Recent advances in statistical modeling were incorporated in the analyses, including the introduction of random effects and nonparametric spatial smoothing components in the Cox proportional hazards model. The findings provide the strongest evidence to date that long-term exposure to fine particulate air pollution common to many metropolitan areas is an important risk factor for lung cancer and cardiopulmonary mortality. Each 10 $\mu g/m^3$ increase in long-term average $PM_{2.5}$ ambient concentrations was associated with approximately a 4%, 6%, and 8% increased risk of all cause, cardiopulmonary, and lung cancer mortality respectively. There was little evidence of statistically significant spatial autocorrelation in the survival data after controlling for fine particulate air pollution and the various individual risk factors. This study has been used as the main estimate in many health burden assessments by the World Health Organization, the Environmental Protection Agency, and the California Air Resources Board. While these estimates are suitable first approximations, especially for the national population, questions about the generalizability of the findings from Pope et al. [2] to California populations have hampered efforts to estimate the benefits of regulatory interventions by the ARB. Further controversies about the applicability of these risk estimates were generated by recent studies suggesting even larger health effects in southern California than in the national study [1].

Improved Exposure Models and Larger Health Effects

A growing body of evidence suggests that refinement of exposures, especially to the within-city or intraurban scale, will associate with larger health effects, probably due to reduced exposure measurement error. Previous ACS studies have relied on between-community central monitor estimates that assign entire metropolitan areas (MA) the same level of exposure. In the Netherlands, Hoek and colleagues [11] demonstrated a near doubling of cardiopulmonary mortality for subjects living near major roads. Nafstad and colleagues [12] reported an increase in male mortality of over 60% for a plausible gradient in exposure to modeled nitrogen dioxide in Norway. These and similar findings summarized elsewhere [1] demonstrated a need to investigate exposures at the intraurban scale within the ACS cohort.

Studies of $PM_{2.5}$ in California have shown that intraurban exposure gradients are associated with atherosclerosis [13] and high risks of premature mortality [1] in California populations. Jerrett et al. [1] observed a tripling of the relative risk for an identical model used in the Pope et al. [2] study. These recent Los Angeles studies have used geostatistical interpolation models that capture regional patterns of pollution well, but may not account for near-source impacts from local traffic and industry due in part to the zip code assignment of address and to the potential over-smoothing of the geostatistical model used to assess exposure. Given the large health effects reported in these and other European studies [11, 14], and more recent American studies [1, 13], a need exists to refine these estimates of intraurban exposure to reduce uncertainties potentially associated with measurement error.

Critical Periods of Exposure

While the Six Cities study and ACS study have demonstrated an association between long-term exposure to particulate air pollution and mortality [2, 4, 5], none of these studies provided an indication of the critical period of exposure responsible for the observed association [15]. Investigations by Zeger and colleagues [16] and Schwartz [17] have shown that mortality cannot be attributed entirely to the effects of short-term peak exposures, which may affect sensitive individuals with pre-existing conditions [18-21]. Krewski and colleagues [22] developed individual temporal exposure profiles for subjects in the Harvard Six-Cities Study by coding the residential histories of those subjects; however, limited population mobility and limited variation in individual time-dependent exposure profiles precluded identification of critical exposure-time windows [23].

The identification of critical exposure-time windows has important implications for establishing time lines for policy interventions that will maximize public health benefits. Although temporal variation in air pollution relative risk estimates was recently examined in several cohort studies [24, 25], the identification of critical exposure-time windows requires information on temporal patterns of exposure at the individual level. Given the regulatory importance of the results, further work to develop individual time-dependent exposure profiles for American Cancer Society (ACS) cohort participants is needed.

Summary of the Rationale and Objectives

In summary, prior research has underscored the need for health effects estimates specific to the California population. To understand the magnitude of potential effects, risk estimates need to be based on pollution variation both between and within cities. Finally, further emphasis on the critical exposure windows is required to guide policy interventions aimed at protecting public health. In the next section we document a comprehensive program of research aimed at addressing these needs and the following objectives:

1. To derive detailed assessments of the health effects from particulate air pollution and other criteria co-pollutants on all-cause and cause-specific mortality in California based on the American Cancer Society Cohort;

2. To investigate whether specific particle characteristics associate with larger health effects through examination of intraurban gradients in exposure to different particle constituents and sources; and

3. To determine whether critical exposure windows exist in the relationship between air pollution and mortality in California.

METHODS

This section summarizes the proposed methods and data to support the investigation of our primary objectives in the California ACS cohort. We begin with discussion of the health data. This is followed by the proposed methods of exposure analysis and finally by the statistical model used to assess the association between particulate air pollution and mortality. Although $PM_{2.5}$ will be our primary focus, we will also assess associations between ozone, nitrogen dioxide, and PM_{10}. Where possible, we will assess associations with speciated data, although the relatively sparse network will make this a challenging task. We have included the examination speciated data at the direct request of ARB staff, and we will therefore work to address this important question to the best of our ability within the constraints of the data available.

Updated Cohort Health Data

The original analysis [5], the HEI sponsored reanalysis [22] and our new research funded by the HEI reported here all have relied on data from the ACS Cancer Prevention Study II (CPS-II), an ongoing prospective mortality study of approximately 1.2 million adults. Cohort participants were enrolled by ACS volunteers in the Fall of 1982 and they resided in all 50 states, the District of Columbia, and Puerto Rico. Most were friends, neighbors, or acquaintances of the ACS volunteers. Enrollment was restricted to persons who were at least 30 years of age and who were members of households with at least one individual 45 years of age or more. Participants completed a confidential questionnaire which included questions about age, sex, weight, height, demographic characteristics, smoking history, alcohol use, occupational exposures, and other characteristics. With the previous analysis the analytic cohort has been restricted to include those who resided in U.S. metropolitan areas within the 48 contiguous states (including the District of Columbia) and within metropolitan areas that had available pollution data. The number of cities for which pollution data are available differs depending on the pollutant, the time period, and quality control criteria used to compile the data. For example, sulfate data from the original analysis is available for 151 metropolitan areas and the number of participants available for the analytic cohort is approximately 550,000.

For this proposal we will utilize the entire cohort from California because of the expanded exposure profiles available from work on the California Teachers Cohort (see below for description). These estimates will empower studies of the entire State of California. This has significant benefits in terms of sample size. For example, if we restricted the analysis to the previous cities included in the ACS pollution studies, we would have only 42,000 subjects. With the extended exposure assessment and geographic scope, we will have 95,112 subjects and 26,183 deaths with the follow-up to 2000. This larger sample will increase statistical power enabling us to detect in some of the specific causes of death for which we have observed large associations, but for which the estimates did not achieve statistical significance by conventional standards (e.g., lung cancer and diabetes). As shown in Figure 1, the cohort is widely distributed across the entire state. Our health effects modeling framework will explicitly account for these trends.

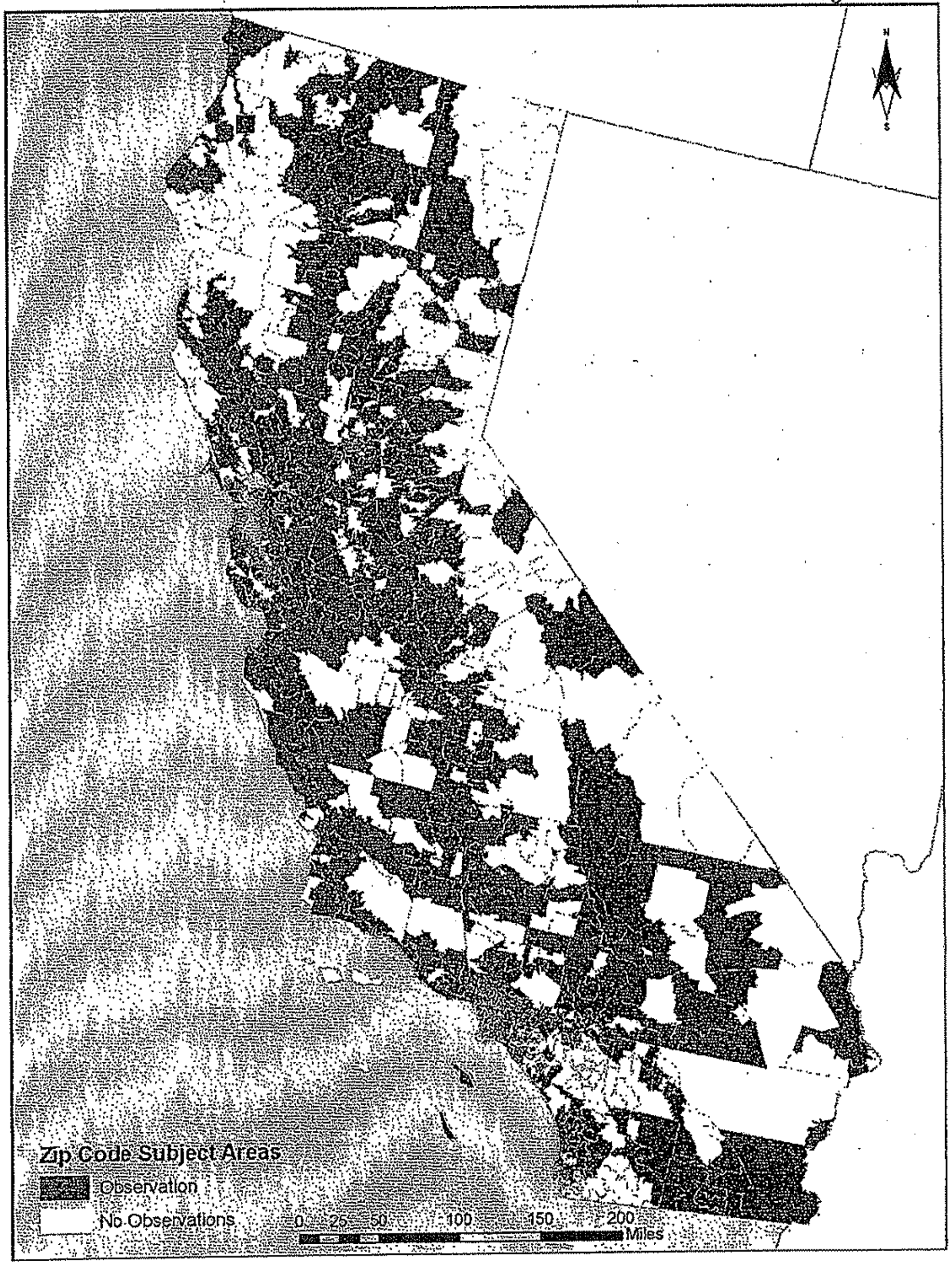


Figure 1. Zip Codes Containing ACS Subjects in California

Mortality of the study participants was ascertained by volunteers in 1984, 1986, and 1988, and subsequently with automated linkage using the National Death Index. This has extended the follow up to 2000 and identified deaths among individuals lost to follow-up. Death certificates or multiple cause-of-death codes were obtained for participants known to have died. For the original analysis [5] and the reanalysis [22], vital status data were only available for approximately 7 years of follow-up (through December 31, 1989). The extended analysis will include vital status data with multiple cause-of-death codes, for approximately 18 years (through December 31, 2000). This extended follow-up yields approximately 3 times more deaths than the 7 years used in the reanalysis, contributing substantially to the statistical power of the study. For this study we will have follow-up through to the year 2000, adding an additional two years to the Pope et al. (2002) study.

Ecologic/Neighborhood Covariates

"Contextual" effects occur when individual differences in health outcome associate with the grouped variables that represent the social, economic, and environmental settings where the individuals live, work, or spend time (e.g., poverty in a neighborhood). It is now widely recognized that such effects may confound or modify the association between air pollution and mortality [26], and we have seen significant confounding in our Los Angeles study [1].

We have already obtained information on neighborhood social confounders for 11,334 zip code areas (ZCA) from the 1979 US Census. Because the 1979 census does not have zip code tabulations readily available, we purchased the entire tape data file and created our own program to extract the census variables. Several variables will be examined in this analysis, including: median household income, 125% of poverty line, percentage of unemployed persons over the age of 16 years, percentage of adults with less than grade 12 education, percentage of homes with air conditioning, household median income, the GINI Coefficient of income inequality, and percentage of population that are not white. We used boundary averaging methods to overlay census information at the census sub-division level and the ZCA level for which we have location information from the ACS subjects. We will only use those ZCAs which contained ACS subjects to more accurately represent the social environment of the ACS participants for metropolitan areas.

Because we were concerned that comparing zip code characteristics between cities does not fully capture confounding, we will also create two other variables for inclusion in the Cox survival models. The first involves aggregating all ZCAs with ACS subjects within a metropolitan statistical area (MSA) to obtain an average estimate of the ecologic confounder. The second will deviate the zip-code specific values from their metropolitan area means. This deviation ensures that all comparisons are made within communities where the social variables are most likely to have interpretable results because cost of living and other factors affecting the comparisons are controlled within cities.

For those variables found to be significant confounders based on the 1979 Census, we will also conduct sensitivity analyses using the 2000 census variables at the zip code scale. These variables are much easier to obtain because they are included in the zip code tabulation file, and 2000 provides estimates that are at the end of the follow up period.

Exposure Modeling and Assessment

Exposure Data

Historical Air Pollution Database

The initial health effects assessment will rely on a database of monthly PM_{10}, O_3, and NO_2 ambient concentrations for California. ARB staff have developed these monthly averages and interpolated them to cover the entire State of California using inverse distance weighting. The monthly values were determined from hourly measurements of gaseous pollutants and every-sixth-day 24-hr measurements of PM_{10} using data completeness criteria (e.g., 75 %) agreed upon in consultation with ARB staff. The principal pollutant database will cover the eight-year period from January 1988 through December 2002 and include the monitoring station data. Assignments will be made by spatial mapping of monthly concentration fields and by matching to the nearest monitoring station's data within a specified distance criteria.

Using the monthly pollutant data discussed above, exposures, for the first time, will be assigned to the subjects' baseline addresses. We have received approval from Drs. Michael Thun and Jeanne Calle to have a GIS consultant, Zev Ross, go on-site and geocode all available addresses. Once geocoded at the ACS in Atlanta, the locational information will be brought by hand to the University of California, Berkeley, where exposure assignments will be completed. Data will then be transported by hand to the University of Ottawa and linked to the master analytical file there for analyses as described below.

$PM_{2.5}$ Database

Routine ambient air monitoring for $PM_{2.5}$ was initiated in 1999 in California; therefore, these data would be available for only a portion of the study period. All previous studies of chronic health effects using the ACS data have relied on single period exposures and assumed the spatial patterns at one point in time during the follow up represent the chronic exposure for the entire follow up. Although this method has produced useful results, questions persist about the accuracy of the exposure assignment, given the underlying assumption of stability in the spatial pattern of exposure.

To refine estimates of long-term exposures to fine particles among the study subjects, we will rely on a historical reconstruction of $PM_{2.5}$ levels throughout California. Analyses were performed by Dr. C. Blanchard to estimate $PM_{2.5}$ levels for years prior to 1999.

This work has produced a database of estimated $PM_{2.5}$ station values and residential assignments analogous to those for the other pollutants addressed above.

We will also assign exposure levels based on statewide interpolations of the monthly pollutant data already developed by ARB for PM_{10}, NO_2 and O_3. After completion of the geocoding for the ACS subjects, we will assign monthly exposures to all subjects based on the baseline address. There are no work or school addresses in the ACS database, so we will be unable to assign multiple time-location exposure profiles. Recent studies have however indicated that on average people spend 68% of their time at home and a large portion of the remaining time at locations near their home.[27] Therefore, assignment of home address represents the most reasonable approximation for personal exposure in the absence of other information from the time-activity budget.

These deterministic surfaces will be augmented with the more advanced land use regression, geostatistical, and Bayesian models to refine exposure assessment and minimize error. These surfaces are described in detail below.

Source Proximity and Speciation Analysis

We will also assign proximity measures of exposure for major freeways and ports in the State. Although we cannot supply exact numbers until address-level geocoding is complete, we have done preliminary analyses based on the Ports of Long Beach and Los Angeles. Within 5 km of the Ports, there are 3840 ACS subjects and 717 deaths, which will allow for testing of individual effects from proximity to these facilities. The proportion around major highways will be much larger.

With further assistance from ARB staff, we will also assign exposures of elemental carbon, organic carbon, metal species, nitrates, and sulfates. These are available through a more limited monitoring network, but the spatial coverage appears sufficient to derive exposure estimates for some of these constituents. We will undertake detailed analysis and assessment of the data supplied to us by the ARB with the intention of assessing constituents and source factors most closely associated with health effects. Dr. Thurston has also recently been awarded funding from the Health Effects Institute (HEI) to assess the particle constituents most closely associated with health effects. He will advise on the interpretation and modeling of these speciated data. Although there is a parallel project funded by HEI, this proposed study will supply unique information because the HEI project focuses solely on between metropolitan area exposures, rather than intraurban exposures. For the speciation analysis, we will develop and detail these analyses in consultation with ARB staff as the extent of the available data becomes more clear. Although the ultimate results are uncertain given the novelty of this approach and the data involved, we understand that the question of which particle species exerts health effects is an important priority for the ARB. We have therefore have tried to address this question directly, although we cannot guarantee the data will be sufficient to determine whether species of particles can show different effects until the data are supplied to us by the ARB staff.

Modeling Exposure Surfaces for Health Effects Assessment

Land use regression (LUR) models will be used for estimating spatial surfaces that represent traffic pollution exposures in our health effects and integrated models. LUR utilizes the pollutant of interest (e.g., $PM_{2.5}$) as the dependent variable and proximate land use, traffic, and physical environmental variables as independent predictors. As illustrated in Figure 2, the method uses measured pollution concentrations Z(s) at locations s as the response variable and land use types W(s) within circular areas around s (called buffers) as predictors of the measured concentrations. Interpolation from monitoring data is informed by local land use and physiographic information to improve prediction over small areas. LUR is particularly well-suited for estimating spatial variation in pollutants likely to have small-area variation [28]. Dr. Jerrett has successfully implemented land use regression models in San Diego [29], Toronto [30] [31], Hamilton [32], Montreal [33], Los Angeles [34], Oakland [35], Long Beach [36] New York City [37], and Vancouver [38]. This extensive experience has demonstrated the viability of LUR in the North American context for predicting both gaseous and particulate matter, with coefficients of determination (R^2) in the range of 0.6-0.85 across the different cities. He is also funded under the EPA and the National Institutes of Health (NIH) to calibrate LUR models for nitrogen oxides and ozone across the existing 16 Children's Heath Study communities. Consequently, an extensive land use database for southern California has already assembled and ready for analysis. Extension of the database to the rest of the California will be undertaken in the first year of this project.

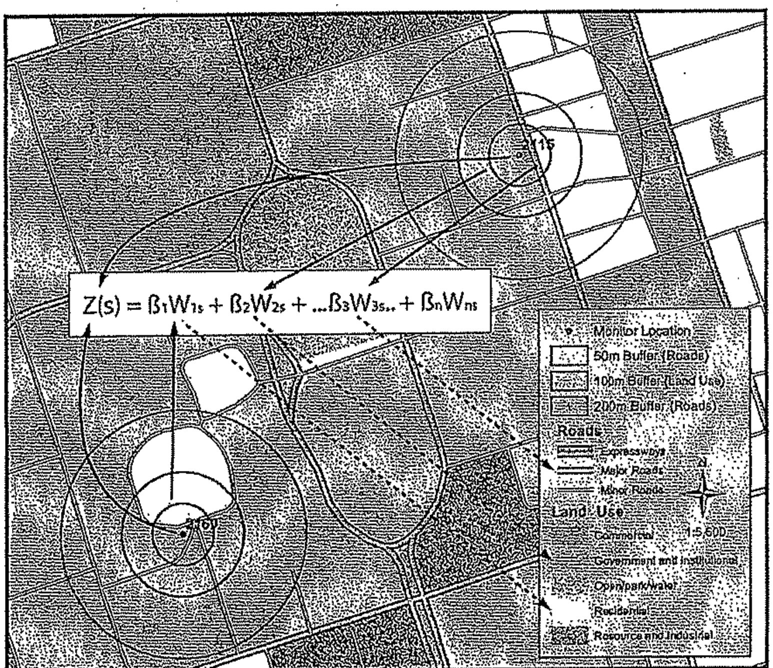


Figure 2. Land Use Regression Illustrated

To implement LUR models, we will calculate the predictor variables as the area and length under a set of neighborhood buffers. All land-use variables are measured in hectares, under various radii buffers, centered on the air pollution-monitoring site. The length of road is calculated, under different buffer distances in two different forms: (1) a circular buffer that extends from the monitoring point of origin to a given radius of, for example, 50 m; and (2) an annulus (donut) buffer from a 50 m radius to a 300 m radius. We will also conduct sensitivity analyses for buffers up to 3000 m for roads and 5000 m for land use. All area and length calculations will be performed using ESRI's Arc 9.2 software (ESRI, Redlands, CA). We will also include traffic counts to derive traffic-to-road-length densities for major roadways, which have been complied already based on the DataMetrics traffic count information available through ESRI (Redlands, CA). Other demographic data from the 2000 census will be used to compute densities of persons and dwellings around the monitoring locations. We will also draw on digital elevation, meteorological data, and remote sensing LANDSAT and MODIS imagery to further inform the prediction of pollutant concentrations. A detailed description of all land use variables currently assembled can be found in Appendix A.

Because the land use regression model requires intensive data inputs, we will calibrate these models to more recent exposures when land use and traffic data are available. Specifically, we will implement models for each pollutant using the 5-year average (1996-2000), which coincides with the end of the follow-up period when land use data will most closely match the digital land use and transportation data. For $PM_{2.5}$ we will use the annual averages from 2000-2001, the first two full years when measurement data are available. We will conduct careful analysis of the residuals to with the Moran's *I* tests for spatial autocorrelation. This will ensure the underlying assumption of independence is maintained and will suggest alternative model specifications that improve prediction accuracy. Assignment of these exposures, similar to earlier ACS studies, will therefore assume a the same spatial pattern of exposure over the entire follow up. Because of the inherent limitations in this approach, we will also implement a space-time modeling, as described below.

Integration of the Land Use Regression with Bayesian Maximum Entropy Kriging

The geostatistical Bayesian Maximum Entropy (BME) estimation method [39] performs interpolation of monitored air pollution data augmented with additional "soft" information from variables such as traffic counts or land use. Under the condition where only observed monitoring data are available the BME method defaults to a more traditional geostatistical method called kriging [40]. Kriging models exploit spatial dependence in the data to estimate the likely value for a random variable Z at unmeasured locations between sampling sites. The spatial dependence can be divided into two categories. First order effects measure broad trends in all the data points such as the global mean, while second order effects measure local variations at short distances between the points. Breaking this down the equation takes the following general form for a random variable Z at location s:

$$Z(\mathbf{s}) = \mu(\mathbf{s}) + \varepsilon(\mathbf{s}) + \varepsilon' \qquad \text{Eq. 1}$$

where $\mu(\mathbf{s})$ equals the deterministic function that describes the "structural" or first order trend component of Z at $\mathbf{s}$; $\varepsilon(\mathbf{s})$ is the stochastic second order effect of the residuals from $\mu(\mathbf{s})$ that vary locally, but are spatially dependent (sometimes called the "regionalized variable"); and ε' represents the residuals that are spatially independent normal terms with zero mean and constant variance. The search for a suitable interpolation model begins with deciding on a function for $\varepsilon(\mathbf{s})$. If we assume that variance of the differences between sites depends solely on the distance between the sites, denoted as $\mathbf{h}$, then the equation for estimating $\varepsilon(\mathbf{s})$ or (semivariance) is given as follows:

$$\psi(\mathbf{h}) = \hat{\text{cov}}(Z(\mathbf{s}), Z(\mathbf{s}+\mathbf{h})) = \frac{1}{2n}\sum_{k=1}^{K_\mathbf{h}}\{Z(\mathbf{s}_k) - Z(\mathbf{s}_k + \mathbf{h})\}^2 \qquad \text{Eq. 2}$$

where, $K_\mathbf{h}$ would equal the number of pairs k of sample points with values of the attribute of interest Z, which are separated by distance $\mathbf{h}$; the semivariance is represented by $\psi(\mathbf{h})$. While executing the interpolation of the point-attribute samples of pollution, experimental variogram models are fit to theoretical distributions. We can adjust this model to incorporate anisotrophic wind patterns.

In regionalized variable theory, two conditions must be met to satisfy the "intrinsic hypothesis": (1) stationarity of difference and (2) stationarity of variance of differences. This intrinsic hypothesis states that once first order effects are accounted for, the remaining variation will be homogeneous and purely a function of distance between the sampled points. If these conditions are fulfilled the first equation can be written as follows to emphasize this hypothesis:

$$Z(\mathbf{s}) = \mu(\mathbf{s}) + \text{E}[\varepsilon(\mathbf{s}) \mid \{\varepsilon(\mathbf{s}i)\},\psi] + \varepsilon' \qquad \text{Eq. 3}$$

where $\text{E}[\varepsilon(\mathbf{s}) \mid \{\varepsilon(\mathbf{s}i)\},\psi]$ is an average of the residuals at the measured sites, appropriately weighted by their distance from the point of interest $\mathbf{s}$ using the semivariance function. Figure 3 represents an example where universal kriging has been used to estimate $PM_{2.5}$ levels in the Los Angeles Basin [1].

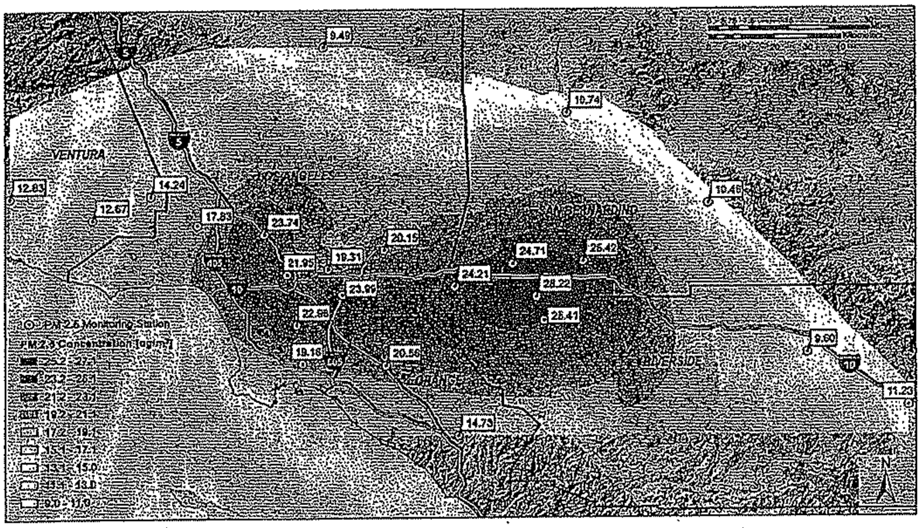


Figure 3: Universal kriging model of 2000 annual average $PM_{2.5}$ in Los Angeles

When additional "soft" information is combined with observed data this can translate into a method which reduces the predictive instability compared to other interpolation methods.

In the case of the ACS cohort, we will combine a theory of space-time dependence under conditions of uncertainty with a methodology of interdisciplinary knowledge synthesis that is expressed in terms of rigorous mathematical formulas [41, 42].

Technical Specification of the BEM Theory and Model

Human exposure research in terms of the spatiotemporal BME theory and technology involves four major stages: adequate conceptualization, rigorous formulation, substantive interpretation, and innovative implementation. Each stage requires an interdisciplinary group effort of scientists familiar and receptive to important science integration goals, extensively discussed in the public health literature. The BME theory, methodological characteristics and computational techniques are discussed in detail in Christakos [43], Christakos *et al.* [42, 44], Yu *et al.*, [45] and references therein. Below we provide a brief review of the main conceptual and mathematical elements of the BME approach.

1. A human exposure system typically involves large numbers of interacting agents. In this context, the attributes of interest include population exposure, incidence rate, mortality, propagation velocity, and population density. Some of the above are emergent properties that manifest the composite geographical-temporal organization of the human exposure system. The *spatiotemporal random field* (*S/TRF*) model of BME aims to study the attributes of the system as a whole and connect them to causal relations and space-

time patterns under conditions of uncertainty. A detailed presentation of the S/TRF theory can be found in Christakos [39, 46]. Christakos and Hristopulos [41] discuss several applications of the S/TRF theory in environmental health sciences.

2. Let $X_p = X(p)$ be a S/TRF representing a human exposure attribute that varies within a specified space-time domain. The $p = (s,t)$ denotes a point in the space-time domain, where s is the spatial location and t the time instant under consideration. The S/TRF model is viewed as the collection of all physically possible realizations concerning the attribute or system we seek to represent mathematically.

3. Pragmatic tools of the S/TRF theory include the spatiotemporal probability density functions (PDF; uni- and multi-variate); the ensemble averages (variograms, ordinary, and generalized covariance functions); and the local scale heterogeneity characteristics (spatial and temporal orders). From a stochastic theory point of view, the S/TRF model is fully characterized by its multivariate PDF, f_{KB}, which is generally defined as

$$P_{KB}[x_1 \leq X_{p_1} \leq x_1 + dx_1, x_2 \leq X_{p_2} \leq x_2 + dx_2, ...] = f_{KB}(x_1, x_2, ...) dx_1 dx_2 ... \quad \text{Eq. 4}$$

where the subscript *KB* denotes the *knowledge base* that BME analysis used to construct the PDF.

4. In spatiotemporal human exposure analysis and modeling, one distinguishes between two major *KB*s:

i. The *general* or *core KB* (denoted by *G*), which includes physical laws, health models, scientific theories that may be relevant to the attributes of the exposure system; as well as theoretical covariance models (ordinary or generalized) previously known to adequately describe the general space-time correlation characteristics of a wide range of human exposure systems (e.g., a human exposure equation may lead to the corresponding covariance equation, which is solved yielding a theoretical covariance model).

ii. The *site-specific* or *specificatory KB* (denoted by *S*), which includes different sources of information about the particular exposure situation. These sources include: *hard* (exact) measurements characterized by a satisfactory level of accuracy and expressed as numerical attribute values across space-time; and *soft* (uncertain) data that include a significant amount of uncertainty (soft data may be provided in forms such as interval values and Gaussian, triangular, uniform, or even custom-defined distributions that approximate local or global data uncertainty in the space-time domain, etc).

5. In light of the above considerations, the BME approach for studying exposure distributions and related health effects is based on the following fundamental set of vectorial equations [42, 43]

$$\int d\chi (g - \overline{g}) e^{\mu^T g} = 0 \quad \text{Eq. 5}$$

and

$$\int d\chi \, \xi_S \, e^{\mu^T g} - A f_K = 0 \quad \text{Eq. 6}$$

where g is a vector of g_α-functions ($\alpha = 1,...,N$) that represents the *G-KB* available concerning the exposure situation (the bar denotes stochastic expectation), μ is a vector of μ_α-coefficients associated with g (μ_α expresses the relative significance of each g_α-function and depends on the space-time coordinates), the ξ_S represents the site-specific KB available, A is a normalization parameter, and f_K is the pdf expressing the final stochastic solution of the system at each space-time point that accounts for the integration of the general and site-specific KBs. The g and ξ_S are often called the BME functions, whereas the unknown in Eqs. 5 and 6 are the functions μ and f_K across space-time. After the space-time distribution of the PDFs f_K has been derived, a variety of human exposure and risk assessment maps can be generated.

This method will characterize the spatial variability of $PM_{2.5}$ more accurately than in previous interpolations that have used the more traditional geostatistical approach (Figure 4). We have implemented the BME technique in the Los Angeles area for the estimation of ambient $PM_{2.5}$. We added soft information from a land use regression (LUR) model [34] to predict $PM_{2.5}$.

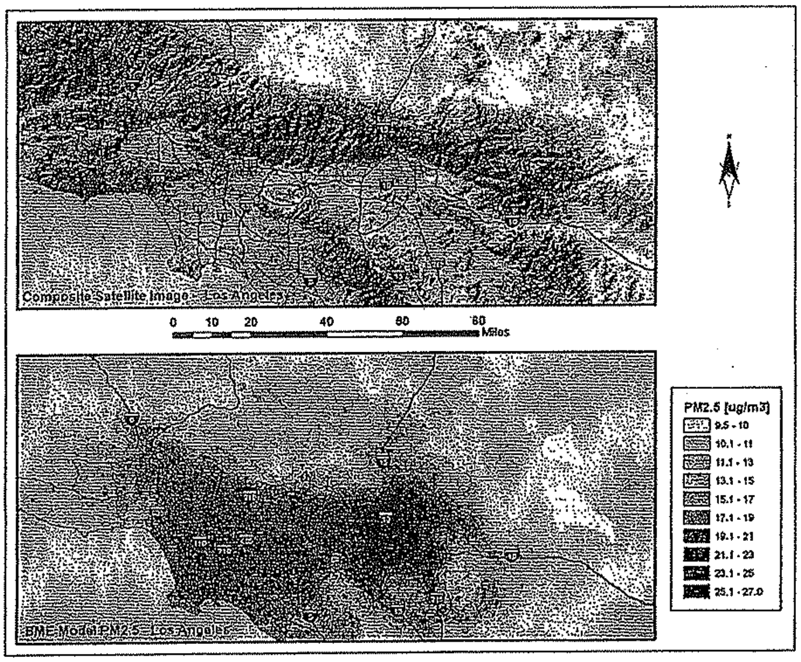


Figure 4: BME estimation compared to physical geography in the Los Angeles area

As the LUR modeling approach uses ordinary least squares regression techniques as a basis for its predictions, we were able to take the 'confidence' in that prediction – the 95% confidence interval (CI) on the predicted values – to be added into the BME interpolation. The upper and lower 95% CI for the LUR predicted values were assigned to an evenly spaced lattice of points with 2500 meter spacing. The results of the BME (Figure 4) when compared to the universal kriging model (Figure 3) produce a more accurate pollution surface, which is confirmed by simulation tests indicating lower MSE and bias in the estimates. This method may also be extended to spatiotemporal interpolation of the monthly values based on the space-time semivariance, known as the "tri-variance" meaning as a function of distance between the samples in both space and time and both together. We will implement these models to compare the results in the health effects assessment with the more basic kriging and IDW models proposed above. These models will be fit using temporal pollution data beginning in 1988 for $PM_{2.5}$, PM_{10}, O_3, and NO_2.

This method will enable us to exploit the full information available in the temporally resolved monitoring data along with the spatial information in the land use regression. After the integrated Bayesian model is fit, we will have the capacity to extract monthly values or aggregated to any temporal domain to derive spatially-representative information over time. By using full information and exploiting spatiotemporal covariance, we will be able utilize all available monitoring data to draw strength from spatial observations that may not be present throughout the entire follow up period.

This method will produce more efficient and accurate estimates of long-term average concentrations though the follow up. It will also be used to assign temporally-weighted exposure concentrations that correctly account for the risk set in the Cox proportional hazards modeling.

Statistical Models of Association for Health Effects Assessment

To examine the association between ambient concentrations of air pollution and longevity in California, we will initially use the standard Cox model to link pollution levels to survival adjusting for potentially confounding risk factors measured at the individual level, such as smoking habits, BMI, and diet, and additional risk factors measured at the five-digit ZIP code level. The baseline hazard function will be stratified by 1-year age groups, gender, and race. This model assumes that all observations are statistically independent, an assumption that will be relaxed in subsequent analyses.

Spatial Cohort Survival Model

Regression models often assume that the response variable is statistically independent over space and time. There is a concern that survival experience may cluster by community or neighborhood. That is, longevity among subjects within the same community or neighborhood will be more similar than subjects in different geographic locales even after controlling for all known and available risk factor information, such as smoking habits, diet, education, and occupation. Furthermore, subjects who live closer together may also share more similar longevity patterns. Lack of statistical control for these factors can both bias the estimate of air pollution effect on health and their associated standard errors. To characterize the statistical error structure of survival data, statistical methodology and computer software that incorporate two levels of spatial clustering (e.g. MSA and ZIP code area – ZCA within MSA) have been developed by our team. At each of the two cluster levels we will incorporate a spatial autocorrelation structure such that the correlation in survival after adjusting for known risk factors is dependent on the distance between clusters. This distance can be defined as Euclidian, adjacency or based on other notions of distance in economic or social terms. The association between concentrations of ambient air pollution and survival can be examined at both the between MSA scale and between ZIP code areas within a MSA spatial scale, thus permitting a simultaneous exposure assessment of health effects at the macro and micro level.

Our model can be expressed mathematically in the form

$$\lambda^{e}(t) = \lambda_0(t) U^{r(e)} \exp(X^{e}(t)\beta) \quad \text{Eq. 7}$$

where $\lambda^e(t)$ is the hazard function for individual e, $\lambda_0(t)$ is the baseline hazard common to all individuals in a stratum, β is a regression coefficient vector, and $X^e(t)$ is a row vector of possibly time-dependent covariate values for individual e and time t. Here, $U^{r(e)}$ represents the random effect for the $r(e)^{th}$ ZCA which contains subject e, with unit expectation and variance given by the sum of the MSA variance (σ^2) and the ZCA variance conditional on the MSA random effect (τ^2).

We assume that given the ZCA and MSA random effects, responses between subjects are independent. The correlation structure of the random effects at the ZCA conditional on the MSA level random effects is specified by the form ρ_N^d, where $0 \leq \rho_N < 1$ is the correlation parameter for ZCAs and d is a measure of spatial association between two ZCAs within a MSA, such as nearest neighbors or Euclidean distance. In a similar manner we assume that the correlation between MSA level random effects is given by ρ_C^d, where $0 \leq \rho_C < 1$ is the correlation parameter for MSAs.

Estimation of the unknown regression parameters and random effect variances under the assumption of no spatial autocorrelation is given by Ma, Krewski and Burnett [47]. This model has recently been extended to include spatial autocorrelation on the random effects (HEI report, 2007). The model is further expanded to accommodate time-dependent covariates. The log-partial likelihood, which forms the bases of parameter estimation, is presented in Appendix B.

For this study we consider time in terms of calendar time. The basic component of the Cox survival model is a comparison of the covariate values of an individual that died and the set of covariates of all those subjects still alive at that death time. These comparisons are summarized over all subjects that die. In the case of air pollution exposure, for those subjects that die, if their exposure tends to be higher than those subjects that are alive at any death time, then a positive estimate of exposure is obtained from the Cox survival model.

The Cox proportional hazards survival model, and our extension to include random effects and spatial correlation, can also include covariates that vary in time. Consider the general form for time dependent air pollution exposure profile

$$z_i(t) = \int_0^t w(s)x_i(s)ds \qquad \text{Eq. 8}$$

where $\{x_i(s); 0 < s < t^{(i)}\}$ represents the exposure history for the i^{th} subject and $w(t)$ is a time dependent weighting function common to all subjects. Here $t^{(i)}$ is the death time of the i^{th} subject or the study determination time if that subject survives until the end of the study. Note that a subject's exposure profile is not defined after the time of death of that subject. If exposure history is assumed to change only at fixed points in time, say every month, then the integral in the above equation can be represented by a weighted sum of the form

$$z_i(t_j) = \sum_{r=1}^{j} w(t_r)x_i(t_r) \qquad \text{Eq. 9}$$

where the t_j are indexing the months of observation. If the weights are all equal to unity, then the relevant exposure profile for the association between air pollution exposure and mortality at time t_j is the cumulative exposure of a subject from the beginning of the study period. If the weighing function is assigned values of zero to all times prior to t_j and unity at time t_j, then $z_i(t_j) = x_i(t_j)$. In this exposure profile, it is assumed that the only relevant part of the exposure history is the current value. An average of previous exposures is defined by setting the weighting function to the inverse of the number of months of observation prior to that time. Other reasonable weighting functions include the past several years or a multiple year period lagged several years prior to the observation time.

As with the standard Cox survival model, a comparison is made between the exposure profile of each subject that died based on their calendar time of death and the exposure profile of all subjects that are still alive at that time. In this manner, the relative risk of death attributable to air pollution exposure can be determined and compared between several exposure profiles giving some indication which profiles are most strongly associated with mortality.

Combining this approach with the BME spatiotemporal model and home locations will reduce exposure error maximally. This method will allow us to assess with correctly specified models whether the dose-response increases or decreases over time. Understanding the temporal dimensions of dose response will supply critical information to time regulatory interventions.

Benefits of the ACS Spatiotemporal Analysis for California

The proposed analysis to extend the ACS intraurban assessment of the particulate air pollution effects on mortality offers many advantages over the existing database of chronic effects research. These advances in the science will reduce critical scientific uncertainties that impede effective policy action intended to improve public health. The specific advantages are documented below.

1. **Improved statistical power to test disease-specific associations.** Some of the causes of death investigated in the earlier ACS analysis of LA and a subsequent follow-up in New York City were elevated but had insignificant effects. Diabetes, a growing public health problem, had relative risks that were greater than 2, but they were insignificant. It is likely that inclusion of all 95,112 ACS respondents will enhance the statistical power for assessing these important disease groups. Likewise, there were elevated risks for "other cancers" beside digestive and lung cancer. These will be examined for specific causes. The larger sample size in the California-wide analysis will assist with assessing these cause-specific associations.

2. **Enhanced locational accuracy with assessment of traffic and near-source industrial or port effects.** The proposed address-level geocoding will permit assessment of whether proximity to roads, highways, or other putative sources – such as the Port of Los Angeles – exerts an effect on survival in the cohort. In a limited number of cohort members (N ~15000) enrolled in the ACS nutritional sub-cohort, we have complete mobility annual mobility records, and these will promote tests of whether exposure error related to mobility influences the size and significance of observed health effects. Based on the findings from the LA study, proximity to roads may have a significant impact on mortality, and the address-level geocodes will allow for assessment of these effects.

3. **Better determination of speciated particle effects.** With the assistance of California Air Resources Board staff, we will also assign exposures to elemental carbon, organic carbon, metal species, nitrates, and sulfates. Where data are available, this will facilitate assessment of particle species most closely related to health effects. The inclusion of other areas beyond LA will increase the heterogeneity in air pollution mixtures available for analysis. Drs G. Thurston and colleagues will also be developing particle factors to assess likely sources as part of a recently awarded Health Effects Institute grant, and they will extend their analytic techniques to the California data.

4. **Increased temporal accuracy in the exposure assignment.** Because this study leverages off the California Teachers Cohort investigation led by Dr. M. Lipsett, we will assign monthly exposures for PM10, all gaseous pollutants, and for reconstructed $PM_{2.5}$ exposures. These estimates are available on a monthly basis, and experience with the Teachers cohort indicates larger effects are present when the longer-term averages are available.

5. **Indication of critical exposure windows for accountability analysis.** In addition to the likely increase in effect size, we will also investigate critical exposure time windows. Through newly developed Cox-Poisson methods, we now have the capacity to assess whether specific time windows of exposure in the follow-up are associated with larger mortality effects. This type of modeling will permit assessment of whether government

programs designed to reduce ambient levels have had effects on the mortality experience in the cohort (although there are many other possible confounding explanations that need to be taken into account such as mobility and differential harvesting of susceptibility in the cohort).

6. **Improved spatial exposure assessment.** The time-resolved and spatially extensive networks of pollution monitors will support advanced geostatistical modeling of exposure. In particular, we will extend the inverse distance weighting exposure assignments from the Teachers study with universal kriging, kriging with external drift determined by traffic density and land use, and fully Bayesian maximum entropy (BME) kriging methods. Dr. Jerrett and colleagues have already extended this method to $PM_{2.5}$ surfaces in LA. The combination of the BME approach with land use and traffic data will enhance the model capabilities, as demonstrated in LA. Dr. George Christakos, inventor of the BME method, will join the research team to supply spatiotemporal estimates of exposure.

7. **Formal assessment of regional heterogeneity in risks.** One of the pressing questions that emerged from the earlier Jerrett et al. [1] analysis was whether LA was unique or representative of broader populations. The proposed extension of the LA analysis to all of California will result in formal assessment of regional heterogeneity through evaluation of whether the residual random effects for counties or zip codes in LA are significantly different than those observed in other parts of the State. This will assist Air Resources Board officials and others with determining the appropriate risk parameters for estimating the benefits of air quality improvements.

8. **Advanced statistical software development for health effects studies.** Drs. Burnett, Krewski, Jerrett and Hughes have worked on development of the spatial random effects Cox-Poisson software for the past four years as part of their recently completed HEI contract. They have derived a working version of the software, but operationally this program is still difficult to use. This project will build on this software and allow for extensions into time varying covariates and for refinement of the user interface and documentation for widespread distribution to other researchers.

In summary, the proposed study will result in assessments of cause-specific deaths; better temporal and spatial exposure representations, including speciated particles and near-source effects; formal heterogeneity assessment of the risks across different regions of California; and an assessment of critical exposure windows. The exposure profiles created will also serve as a major resource for future investigations of the health effects related to air pollution across California.

PROJECT MANAGEMENT AND INVESTIGATORS RESPONSIBILITIES

Dr. Jerrett will lead the overall project management and scholarly decision-making. He will also supply expert guidance on the spatial aspects of the exposure and health effects modeling. Drs. Krewski, Burnett, Shi, and Hughes will coordinate and implement management of the highly confidential data file and the statistical analysis of health effects using the Cox and Random effects Cox model. Drs. Krewski and Burnett have outstanding international reputations for the statistical analysis of complex health data in air pollution research. Dr. Hughes is an expert in mathematical programming, and Dr. Shi has been the principal statistician working with the ACS data for air pollution studies since 1998. Dr. Jerrett has worked closely with all the team members noted above since 1999, when he began working on the Reanalysis Project.

Dr. Pope will supply expert guidance on the interpretation and analysis of statistical modeling and air pollution epidemiology. As the original lead author on the American Cancer Society study and many other seminal works in air pollution research, Dr. Pope is one of the world's most widely cited and recognized air pollution experts.

Drs. Calle and Thun will collaborate with Dr. Krewski to ensure continued access to the ACS data. Drs. Calle and Thun will also comment on and revise all papers before publication, adding expert knowledge in Epidemiology and Medicine.

Dr. Thurston, New York University, also internationally recognized for his work in air pollution epidemiology, is currently working on a Health Effects Institute-funded analysis examining the role of particle characteristics in the ACS cohort nationally. He will supply guidance on formulating and interpreting the exposure metrics for the speciated analysis.

Dr. Christakos, San Diego State University, will lead the spatiotemporal exposure modeling. He is an internationally recognized expert in spatiotemporal modeling. He will hire a postdoctoral fellow to assist with implementation and will work closely with Dr. Jerrett and Mr. Beckerman in deriving the exposure measurement. Mr. Beckerman is expert in GIS and related mathematical modeling and he will begin an M.S. degree with Dr. Jerrett and will base his thesis on this project. He will perform much of the land use regression modeling for his thesis (with emphasis on developing the statewide land use regression model) and perform all joins to the existing exposure data.

Mr. Ross has extensive experience with land use regression. His role will be extending the work he and Dr. Jerrett are already doing to calibrate land use regressions in southern California to the entire State. Mr. Ross has already calibrated land use regressions for Alameda County, San Diego County, New York City, and the 16 communities associated with the Children's Health Study. He will lead the data compilation. Mr. Ross will also work on-site in Atlanta to geocode the 95,112 records available for analysis.

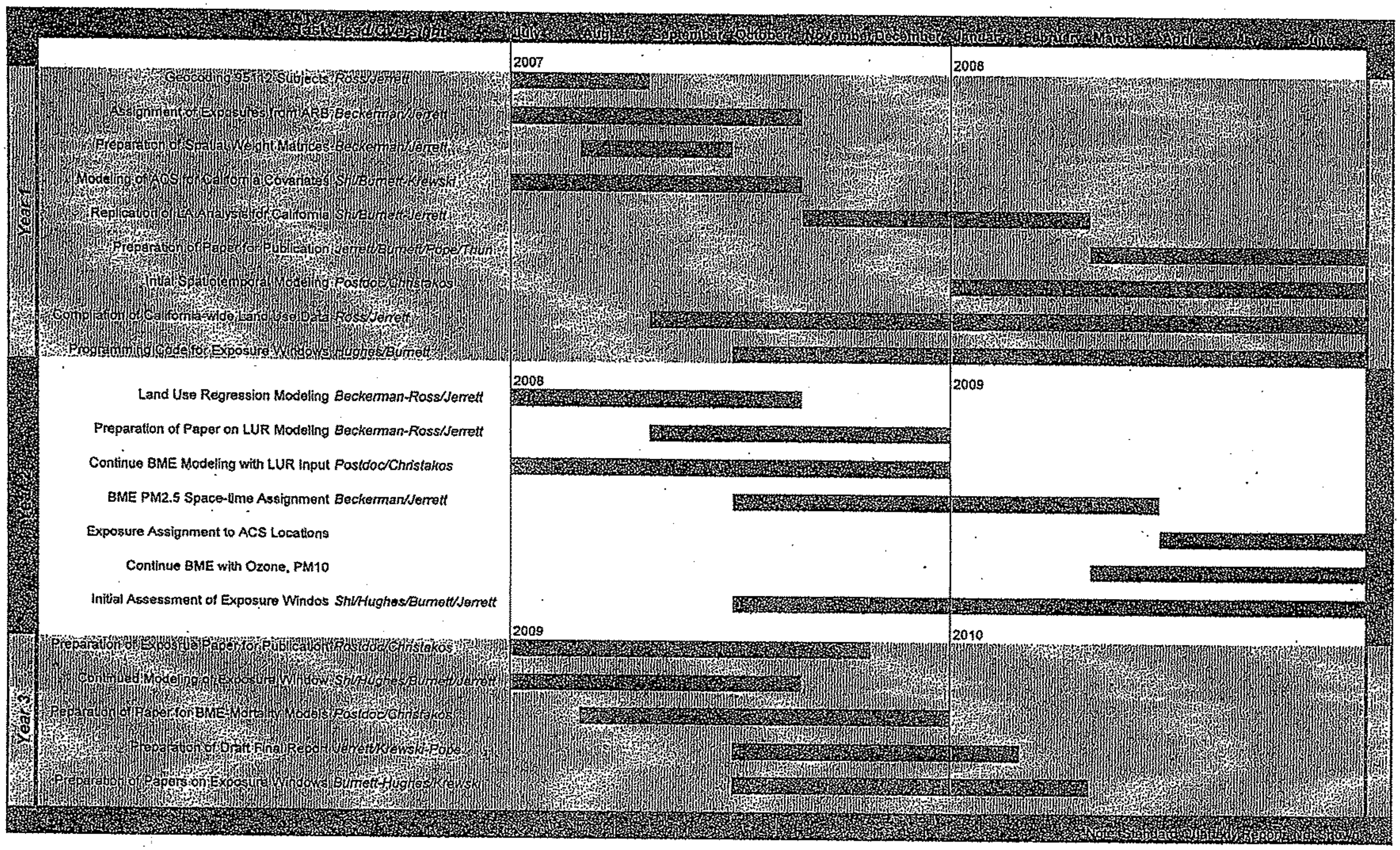
SUMMARY OF WORK PLAN

We recognize the urgent need for statewide estimates of mortality effects. We will therefore put as our highest priority delivery of California-wide estimates, with a secondary emphasis on sophisticated exposure modeling and on understanding critical exposure windows.

Under this broader prioritization, this section summarizes the stages of research and their timing for the ACS cohort investigations of the association between ambient air pollution and mortality in California. The intent here is show the time line of deliverables and responsibilities attached to associated tasks. These are summarized in a Gantt chart on Table 1.

Table 1: Gant Chart summarizing the project schedule

Project Schedule for Jerrett et al. Spatiotemporal Analysis of Air Pollution and Mortality in California



Year 1

Continued Analyses of Morality Effects for the ACS Cohort Analyses of California

For the ACS cohort, we will conduct similar analyses to the earlier Los Angeles study, but covering all of California. For this study we will enhance the exposure profiles of the ACS by linking the zip code assignment to the pollution exposure assessments compiled for the California Teachers study.

Geocoding of Individual Exposures

Mr. Ross will travel to Atlanta in the first two months of the grant. He will work on-site for 3 one-week intervals, returning home twice. He will be assisted by Dr. Calle in accessing the data base.

During this period, the exposure surfaces will be supplied by ARB staff and assigned by Mr. Beckerman in the first four months of grant. These will be assigned to both the zip code and the home address. To supply surfaces for rapid analysis, Mr. Beckerman will assign zip code exposures first.

Modeling of the cohort will be conducted by Dr. Yuanli Shi, University of Ottawa has been the primary data modeler for the Reanalysis, the Pope et al. study, and the Jerrett et al. study. Dr. Rick Burnett, University of Ottawa and Health Canada, will oversee implementation and analysis of the spatial random effects models (his time will be donated to the project as part of his position at Health Canada), and Dr. Shi will work under the direct supervision of Dr. Krewski. Mr. Hughes will continue to refine the random effects program for different spatial connectivity matrices and will supply expert programming guidance, which will be used for the individual-level analysis at the geocode scale and over time windows. The first four months will be devoted to refining the covariates for the California population and to understanding the underlying spatial structure of the data.

After delivery of the zip code assignments of exposure by Mr. Beckerman, the Los Angeles analysis will be replicated for the statewide population. This will occur over the next four months. In the remaining four months of year 1, Dr. Jerrett and colleagues will draft a paper for submission to a high-impact scholarly outlet.

Improved Exposure Analysis

After initial geocoding and assignment of the annual and long-term averages from the Teachers study, we will focus on improving exposure assessment models. Dr. Jerrett will work closely with Mr. Ross and Mr. Beckerman to collect statewide land use, transportation and related data. They will extend the work already completed in southern California to the entire statewide network for $PM_{2.5}$ (based on actual exposures).

In the second half of the year, Dr. Chistakos and his TBN postdoc will begin working with the temporal PM_{10} and $PM_{2.5}$ data. Their work will focus on estimating the basic spatiotemporal structure of the data, which will be integrated with the advanced exposure models in Year 2.

Year 2

Improved Exposure Modeling and Health Analyses
The main foci in year 2 will be on derivation of the Bayesian Maximum Entropy and the kriging with external drift models, with the drift specified by the land use regression.

Although the earlier ACS cohort has produced promising initial results, the exposure metrics used constitute a basic form of spatial interpolation. The exposure error imparted in these interpolations may reduce the size and significance of observed health effects. Given the potential importance of these findings, a need exists to examine the impact of more refined exposure metrics such as geostatistical kriging, universal kriging with external drift, and spatiotemporal Bayesian Maximum entropy kriging. All methods have been successfully implemented in the Los Angeles context, but their extension to the entire state and to sub-regions would enhance the exposure profile of the California-wide study.

After derivation of the land use regression models in the first quarter, Dr. Christakos will begin modeling using the predicted land use regression equation to estimate the BME models. Mr. Ross and Dr. Jerrett will implement a universal kriging model with external drift to complement this effort.

Mr. Beckerman will overlay the land use regression models on the home addresses of respondents. These will be used along with the inverse distance weighting estimates to improve exposure assessment for the cohort.

Dr. Jerrett, Mr. Beckerman, and others will prepare a paper for publication summarizing the land use regression modeling.

After assignment, data will be delivered to the team at the University of Ottawa for analysis. The LA analysis will be replicated with the improved exposure assessment and locational accuracy.

As with the results from Year 1, Dr. Jerrett and colleagues will prepare a paper summarizing the results.

During this year, Drs. Hughes, Burnett, Christakos, and Jerrett will continue formulating the critical time windows analysis.

Year 3

Time by Pollution Interaction Analysis of the ACS Cohorts

In Year 3 Dr. Christakos will complete the BME modeling and supply exposure estimates. He will lead the preparation of a paper summarizing the exposure modeling.

After supplying the exposure surfaces to Dr. Jerrett, exposures will be assigned quarterly from 1988 onward. The exposures will then be brought to Ottawa for modeling with the exposure windows framework.

In tandem with this approach, we would also investigate critical exposure time windows, using the newly developed Cox-Poisson Random Effects program, which allows for time by pollution interactions. Although temporal variation in air pollution relative risk estimates was recently examined in several cohort studies overall, the identification of critical exposure-time windows requires information on temporal patterns of exposure at the individual level.

Drs. Burnett and Hughes will work with Dr. Jerrett to implement the fully integrated time windows analysis. This analysis will be published in a high impact journal.

Dr. Jerrett and colleagues will prepare the final report and submit this to the ARB for review in the final six months year 3.

Deliverables

This section follows a model established with the California Teachers Cohort. Unless otherwise specified below, the following deliverables shall be provided to ARB staff prior to the end of this contract for this contract to be deemed complete, and must be in accordance with Exhibit E of this contract. All analyses specified in Appendix C will be considered deliverables for the final contract.

1. **Progress reports.** Project staff will have in-person or telephone meetings with ARB staff monthly and prepare quarterly written progress reports of 5 pages or less.

2. **Report writing.** We will prepare a draft final report 6 months before the end of the contract on the results of this analysis consistent with the ARB Final Report Guidelines. We will submit a final report within 45 days of receipt of both ARB's and the Research Screening Committee's comments on the draft final report.

3. **Manuscript preparation.** We intend to prepare three or more manuscripts for publication in peer reviewed journals. We will also submit an interim progress report after the first 18 months of the contract documenting the results of our statewide analysis of the replication of the Los Angeles study titled, "Spatial analysis of air Pollution and Mortality in Los Angeles" resulting from exposure assessment using IDW and Kriging modeling and the zip code assignment. This will be done in parallel with preparation of

the final report. ARB shall be provided with a 15-day period to provide comments on any manuscript before it is submitted for publication in a peer-reviewed journal. We will incorporate appropriate comments and changes provided by the ARB within the 15-day period.

4. **Presentation to Air Resources Board staff.** We will present the results of this investigation to ARB staff as a technical seminar at a time and location to be agreed upon with ARB staff.

5. **Documentation and data files.** We will provide ARB with the following documentation and data files upon completion of the project:

(i) Logs from the statistical programs used to generate the data summaries and tables contained in the Final Report. These logs will be provided both in electronic and hard copy formats.

(ii) Documentation of the steps taken to generate the exposure estimates for exposure assignment (as noted above these will take the form of peer-reviewed articles). This information will be provided in both electronic and hard copy formats.

(iii) Two electronic datasets consisting of variables utilized in the creation of the land use exposure estimates.

We will not provide to ARB: (i) files containing confidential information or data including variables developed for other research involving the ACS cohort or any other means by which individuals in the cohort may be identified (such as geocoded locations of exposure assignment), or (ii) proprietary data, databases, or software utilized in this project.

Within four months before the completion date of this project, the investigators and ARB staff will meet to decide jointly whether any additional computer files or documentation generated uniquely for this contract would meet ARB staff's objective of understanding the analytical logic of this project. If so, we will provide such files or documentation, subject to: (i) the limitations of confidentiality and proprietary information noted above, and (ii) the proviso that sufficient funds remain in the budget to support any additional work required to provide these files or documentation to ARB.

RELATED STUDIES

In 2002 the Health Effects Institute [8] funded an extended spatial analysis of the American Society Cohort, and the findings of this extended analysis and associated studies have further emphasized the need to clarify outstanding scientific issues. All of the investigators listed on this application have participated actively in this study. The research program addressed the following three key questions:

1. Do social, economic, and demographic ecologic variables confound or modify the relationship between particulate air pollution and mortality?

The analysis of ecologic covariates at multiple scales has led to greater understanding of the potential confounding and modifying effect of these variables on the air pollution-mortality association. While the reanalysis suggested that these variables are unlikely to exert a significant confounding influence. Unresolved questions about scale and the construct validity of the variables used will be addressed directly with the extended analysis that focuses on mobile scale hierarchies of effects, and operational variables - derived from the principal components - that measure the combined effect of many ecologic confounders at once.

2. How can spatial autocorrelation and multiple levels be taken into account within the random effects Cox models?

The standard Cox regression model commonly used in the analysis of cohort mortality data is based on the assumption that individual observations are independent. Due to the presence of spatial autocorrelation induced by complex spatial patterns in the ACS data, this assumption was shown not to hold in Phase II of the Reanalysis. Ignoring such spatial autocorrelation has important implications with respect to bias and precision of model-based estimates of risk. In Phase II, a random effects Cox regression model was developed to take into account spatial patterns in the data that could be described at either one (e.g., city) or two (e.g., county and city) levels of clustering. Computer software for efficiently fitting the random effects Cox model was also developed. In Phase III, a multi-level random effects Cox model capable of handling more than two levels of clustering is developed. This extended random effects Cox model permits our team to explore much more complex spatial patterns in the ACS data, leading to improved estimates of risk that can be used in this proposed study.

3. What critical exposure time windows affect the association between air pollution and mortality?

The overall objective is to develop individual time-dependent profiles for a subset of the ACS cohort to determine what critical exposure time windows are most relevant for the association between air pollution and mortality from all causes, cardiopulmonary mortality, and lung cancer mortality. Whereas virtually no information on population mobility in the ACS cohort was available to the reanalysis team in Phase II, the additional follow-up of the ACS cohort includes information on residence changes within the CPS II Nutritional Cohort (n=184,174), established in 1992 as a subgroup of the larger CPS II. As in the Harvard Six Cities study, residence histories were used to develop time dependent exposure profiles by matching residences to particulate air pollution monitors at the metropolitan area (MA) level. The construction of the time dependent exposure profiles make use of national exposure data developed by Dr. George Thurston and colleagues at New York University.

4. A subsequent aim was added to the study with supplementary funding awarded through a competitive process: To examine what impact refinement to the exposure estimate at the intraurban scale will exert on the size and significance of health effects. Increasing evidence suggests that refinement of exposures, especially at the within-city or intraurban scale, will associate with larger health effects, probably due to reduced exposure measurement error. Hoek and colleagues [11] demonstrated a near doubling of cardiopulmonary mortality for subjects living near major roads. Nafstad and colleagues [12] reported an increase in male mortality of over 60% for a plausible gradient in exposure to modeled nitrogen dioxide. These and similar findings summarized elsewhere [1] demonstrate a need to investigate exposures at the intraurban scale within the ACS cohort.

A report summarizing these findings is nearing completion, with many papers already published or in press (see below for a summary of the papers).

Other Studies of Note

Drs. Jerrett, Burnett and Hughes have also served as a PI, CI or consultants to many of the leading cohort studies, including: The Children's Health Study and a subsequent NIH follow up to this study (as Co-I), an EPA-STAR grant to examine the role of exposure measurement error in the estimation of health effects (as PI); consultant to the California Teacher's Cohort and the Netherlands Nutritional and Cancer Cohort (as consultant); and on a Canadian Institutes of Health Research Cohort study of traffic pollution in relation to mortality (as PI).

Drs. Thurston, Krewski, Pope, Burnett, Shi, and Calle are all coinvestigators or consultants to a project recently funded by the Health Effects Institute to examine mortality risks in relation to different particle characteristics. Dr. Thurston will employ similar methods to derive factors of exposure representing different sources on this current study.

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APPENDIX A

Description of Land Use Variable used in the Land Use Regression

For our existing studies in Southern California, we calculated more than 50 different traffic, land use and demographic variables within buffers of 50, 100, 200, 300, 400, 500 and 1000 meters. All vector-based layers were projected to the Universal Transverse Mercator coordinate system zone 10 and 11 to match monitoring locations. To minimize distortion associated with projecting raster-based layers, we calculated all variables based on raster layers in the Albers Conical Equal Area projection. Table A outlines data sources and associated metadata.

Table A: Census, emission, land use, and transportation metadata and sources

Type	Name	Format	Source	Scale/Resolution	Years of Data	Year Published
Census	(Block Groups)	Polygon	Census Bureau	1:100,000	2000	2000
Elevation	(National Elevation Dataset)	Raster	USGS	30m	1999	1999
Emissions	(NEI Point)	Point	EPA	1:100,000	2002	--
Landuse **	(NLCD)	Raster	USGS	30m	2001	2006
Landuse	(Urban Imperviousness)	Raster	USGS	30m	2001	2006
Landuse	(Tree Canopy)	Raster	USGS	30m	2001	2006
Landuse	(Vector-Various)	Polygon	Multiple municipal sources	Various	2006	2006
Other Transportation	(Airports)	Point	BTS	1:100,000	2006	2006
Other Transportation	(Runways)	Polyline	BTS	1:100,000	2006	2006
Other Transportation	(Water Shipping Lanes)	Polyline	BTS	1:100,000	2006	2006
Other Transportation	(Railways)	Polyline	BTS	1:100,000	2006	2006
Roads	(TeleAtlas)	Polyline	TeleAtlas	1:24,000	--	--
Roads	(StreetMap)	Polyline	ESRI	1:100000	2005	2005
Traffic	(TeleAtlas)	Polyline	TeleAtlas	1:24,000	--	--
Traffic	(Bus Analyst Pt)	Point	ESRI	1:24,000	1978-2003	2005

** 2001 has not yet been released for all of CA, but is expected soon

Census

Using Census 2000 Summary Files 1 and 3 we calculated total population, total urban population, total population inside urbanized areas, total population inside urban clusters, total rural population, total occupied housing unites and the aggregate number of vehicles available for each buffer. All census variables were calculated at the census block group level. A block group's contribution to calculated total values was proportional to the block group's area located that intersected the circular buffer.

Road Density and Road-Related Variables

Road density represents the total length of road within a given buffer. All roads in these calculations are treated as polylines (see the land use discussion below for variables representing the area covered by roads). Road density was calculated using three different data sources including a high resolution TeleAtlas layer and two national-level road networks including the National Highway Planning Network and the Highway Performance Monitoring System. The national-level datasets were used primarily to validate the TeleAtlas layer. In addition to overall road density, we also calculated road density seperated by six functional classes in the TeleAtlas data (interstates through local roads). Finally, we calculated the minimum distance to the nearest limited access major highway (functional class 1).

Traffic Data

Four sources of data were used to generate traffic measures at each subject location at the various buffer sizes. TeleAtlas traffic estimates at the road link level were used as the primary source of information. Using the TeleAtlas data, we calculated total overall traffic as well as totals categorized by light duty and heavy duty vehicles. In a similar fashion to the road density calculations, we used the National Highway Planning Network (NHPN) and the Highway Performance Monitoring System (HPMS) data to calculate traffic densities. For all three of these polyline layers – Teleatlas, NHPN and HPMS – traffic variables were calculated by multiplying the length of each segment within the buffer by the traffic assigned to the segment. The final source of traffic data comes from traffic counts provided by DataMetrix. These traffic counts, the majority of which were calculated between 1990 and 2000, are provided as spot counts (points) rather than link assignments (lines). Given that not all roads were sampled in the DataMetrix data, a total traffic variable is not practical, instead we calculated mean traffic concentrations based on the point traffic data for all buffers.

Raster-Based Land Use Data

Three different raster-based land use layers from the US Geological Survey were used to generate variables for the land use regression. The national land cover data layer provides a consistent 30 x 30m resolution coverage of the entire United States and was used to calculate the total area of agricultural, barren, green, developed, high density residential, water-based and industrial land uses. The other USGS layers allowed us to calculate average urban imperviousness and average tree canopy density for all subjects using the full suite of buffer sizes.

Vector-Based Land Use Data

Vector-based data provides much higher resolution information on land use. To generate vector-based land use variables we collected four different layers – when combined – cover the entire extent of the sampling locations. These include a Southern California Association of Governments layer that covers Los Angeles, Ventura, Orange, Imperial, Riverside and San Bernardino Counties; a layer that covers San Diego from the San Diego County Association of Governments; a Santa Barbara parcel-level layer with land use attributes; and a land use layer that covers the City of Atascadero. These layers were used to calculate the total area covered by land use in the following categories: agricultural, commercial, governmental, industrial, open, park, transportation, airport, water and electrical corridors.

Emissions

We combined shapefiles and raw data from the US EPA's National Emissions Inventory (2002) to calculate the total number of point emitters as well as the total NOx, $PM_{2.5}$, PM_{10} and volatile organic compounds emitted by point sources within each of the buffers.

Other Transportation Data
Using data and shapefiles from the Bureau of Transportation Statistics' North American Transportation Atlas we also calculated the total number of airports and heliports, the density (length) of airport runways, density of railroads and density of high-traffic railroads.

Elevation
Finally, we used the USGS's National Elevation Dataset at 30 x 30m resolution to calculate the elevation of all monitor locations.

APPENDIX B

Likelihood Functions for the Cox Model with Random Effects and Time-Dependent Covariates

Edward Hughes

Cox Model

We consider the Cox proportional hazards model

$$\lambda^e(t) = \lambda_0(t)\exp(X^e(t)\beta) \quad \text{Eq. 10}$$

where $\lambda^e(t)$ is the hazard function for individual e, $\lambda_0(t)$ is the baseline hazard, common to all individuals in a stratum, β is a regression coefficient vector, and $X^e(t)$ is a row vector of covariate values for individual e and time t. We will consider *clusters* and the random effects associated with them. By a cluster is meant a subset of individuals, usually defined by individual attributes such as city of residence state, etc. Often the clusters will be arranged in a multi-level hierarchy (e.g. zip-codes within cities), but for our purposes here it is sufficient to consider only the clusters at the finest level, the "leaf" clusters. We assume that the leaf clusters are mutually exclusive and jointly exhaustive of the individuals. In the example given, zip-codes (more precisely, the sets of individuals having the same zip-code) would constitute the leaf clusters. By $r(e)$ we mean the leaf cluster containing the individual e. Associated with each cluster r is a random effect, written either $U(r)$ or U^r, which is a positive random variable with expected value 1 and a finite variance.

We can modify the Cox model to accommodate random effects as

$$\lambda^e(t) = \lambda_0(t)U^{r(e)}\exp(X^e(t)\beta) \quad \text{Eq. 11}$$

This differs from the notation in some sources [48] in placing the random effect as an extra positive coefficient of the exponential factor, rather than as an extra term in the exponent. The difference is purely notational.

The modern theory of the Cox model is developed in terms of counting processes [48, 49], which facilitates both theoretical and computational efforts. Consider first the case of unstratified data, and no ties (simultaneous events). For the Cox model with no random effects, the partial log-likelihood is given by

$$\log(p\ell(\beta;Y)) = \sum_{e\in E}\int_0^\infty\left[\delta(e,t)X^e(t)\beta - \log\left(\sum_{g\in E}\delta(g,t)\exp(X^g(t)\beta)\right)\right]dN_e(t) \quad \text{Eq. 12}$$

where: E is the set of all individuals in the sample, $\delta(e,t)$ is 1 if individual e is at risk and under observation at time t, and $N_e(t)$ (the counting process) is the number of events suffered by individual e up to (and including) time t. The log-likelihood expression given here is essentially the same as Therneau and Grambsch [48], formula (3.3).

To add random effects to the model, we let $U^{r(e)}$ denote the random effect associated with the leaf-cluster $r(e)$ containing individual e. The log partial likelihood conditional on all random effects is

$$\log(p\ell(\beta;Y|\mathbf{U})) = C + \sum_{e\in E} \int_0^\infty \left[\delta(g,t)(\log(U^{r(e)}) + X^e(t)\beta) - \log\left(\sum_{g\in E} \delta(g,t) U^{r(g)} \exp(X^g(t)\beta) \right) \right] dN_e(t) \quad \text{Eq. 13}$$

The constant C includes various terms, and is independent of the regression coefficients and the random effects, so is irrelevant to their estimation. We can write the log-likelihood expression out explicitly as a sum over event times and individuals, interchanging the summations over individuals and times. Let $(t_1, t_2, \ldots, t_q)$ be the list of all distinct event-times (the times at which any $N_e(t)$ has a jump). Then

$$\log(p\ell(\beta;Y|\mathbf{U})) = C + \sum_{h=1}^{q} \left[\sum_{e\in D_h} [\log(U^{r(e)}) + X^e(t_h)\beta] - \log\left(\sum_{g\in R_h} U^{r(g)} \exp(X^g(t_h)\beta) \right) \right] \quad \text{Eq. 14}$$

where R_h is the risk set of event-time t_h, the set of individuals at risk and under observation at time t_h, and D_h is the set of individuals actually experiencing an event at time t_h.

We have stated the log likelihood under the assumption of no stratification and no ties. To accommodate stratification, we note that the full log-likelihood is simply the sum over strata of the single-stratum log-likelihoods. If there are ties, we use the Breslow-Peto approximation, and letting s denote strata, and t_{sh} the event-times of individuals in stratum h, the log-likelihood is

$$\log(\ell(\alpha,\beta;Y|\mathbf{U})) = C + \sum_{s=1}^{a} \sum_{h=1}^{q} \left[\sum_{e\in D_{sh}} [\log(U^{r(e)}) + X^e(t_{sh})\beta] - m_{sh} \log\left(\sum_{g\in R_{sh}} U^{r(g)} \exp(X^g(t_{sh})\beta) \right) \right] \quad \text{Eq. 15}$$

where m_{sh} is the multiplicity of the event-time t_{sh}, i.e. the number of events occurring in stratum s at time t_{sh}.

Poisson Form

As shown by Whitehead [47, 50], the expression (Eq. 15) is equivalent to the log likelihood of a Poisson generalized linear model. This is the form we use for computation. To define it, we introduce values $\{\alpha_{sh}\}$ for each stratum s and event-time t_{sh}. We also define event-indicators $Y(e, t_{sh})$, for all individuals e and all event times t_{sh} such that e is in stratum s, and is at risk and under observation at time t_{sh}: $Y(e, t_{sh})$ is 1 if individual e has an event at time t_{sh}, and 0 otherwise. We postulate that, given random effects $\{U^r\}$ for all leaf-clusters r, the values $Y(e, t_{sh})$ are conditionally independent, and have conditional distribution .

$$Y(e,t_{sh})|U \sim \text{Poisson}(U^{r(e)} \exp(\alpha_{sh} + X^e(t_{sh})\beta)) \quad \text{Eq. 16}$$

The conditional log-likelihood for this Poisson generalized linear model, given the random effects, (ignoring an additive constant) is

$$\log(\ell(\alpha,\beta;Y|\mathbf{U})) = \sum_{s=1}^{a}\sum_{h=1}^{q}\sum_{e\in R_{sh}} \left[[\log(U^{r(e)}) + \alpha_{sh} + X^e(t_{sh})\beta]Y(e,t_{sh}) - U^{r(e)}\exp(\alpha_{sh} + X^e(t_{sh})\beta)\right] \quad \text{Eq. 17}$$

It is this expression we use to develop the computational algorithms. We must maximize over both the β-values and the α-values. The proof of equivalence with (1) is straight-forward, and is given by Whitehead [50], Ma et al [47], and Hughes [51]. The same formula in the notation of Ma et al [47] is

$$\log(\ell(\alpha,\beta;Y|\mathbf{U})) = \sum_{s=1}^{a}\sum_{h=1}^{q}\sum_{(i,j,k)\in R_{sh}} \left[\left(\log(u_{i,j}) + \alpha_{sh} + \mathbf{x}^?_{i,j,k,h}\beta\right)Y^{(s)}_{i,j,k,h} - u_{i,j}\exp(\alpha_{sh} + \mathbf{x}^?_{i,j,k,h}\beta)\right] \quad \text{Eq. 18}$$

Estimation using this model is done by a variant of the EM algorithm: the log-likelihood is maximized (with respect to α and β) for fixed random effects, and then the random effects are predicted for the new α and β using the BLUP method; this alternation is iterated until convergence. Details are given in Hughes [51].

APPENDIX C - EXPOSURE MODELING FOR HEALTH ASSESSMENT

Spatiotemporal Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort

All particle and gaseous pollutants exposure metrics that will be developed as described below (IDW, Kriging, Kriging/LUR w external drift, and full BME Kriging) will then be analyzed to determine the relative risk for all cause and cause-specific mortalities. The health analysis will be done using the standard Cox model, newly developed Cox-Poisson Random Effects model and Spatial Cohort Survival model.

Dr. Jerrett, Principal Investigator, has proposed a comprehensive and rigorous program of modeling spatiotemporal exposures as described in this Appendix C. Specifically, Dr. Jerrett will implement all the modeling exercises outlined in Tables 1 though 5 below. To implement these models, ARB will supply analysis-ready pollution data with accurate geographic location data on the air pollution monitoring sites to be used for exposure assessment, including historical location information. Full meta data explaining how the air pollution data and locations were derived will be supplied to the investigators with the data prior to analysis. In addition, Dr. Jerrett will develop state wide exposures surfaces from all the modeling exercises outlined in Tables 1 through 5 and will link these surfaces to health data if these surfaces are scientifically defensible. For purposes of this Appendix C, "scientifically defensible" means that it survives peer review of experts in the field selected in consultation with ARB staff. ARB understands that the investigators may not be able to develop state wide exposures surfaces with kriging, kriging with LUR external drift, or BME Kriging models (collectively "kriging models") for a specific pollutant if available data cannot support these kriging models for that pollutant. For example, the external drift model will only function if the investigators have an external drift that leaves residual spatial autocorrelation. In other words, the investigators need to have a land use regression that leaves spatial autocorrelation in the residuals to utilize the kriging with external drift. Nevertheless, the investigators will attempt all three kriging models and thereafter determine whether scientifically defensible exposure surfaces can be developed with these kriging models. In the event the statewide exposure surfaces for a specific pollutant using these kriging models cannot be developed because one or more of the surfaces would be scientifically indefensible, the final report will contain a section justifying and documenting in detail the specific reasons for the exclusion of these exposure surfaces and kriging models. The documentation will include the results of all attempted modeling, including any modeling that resulted in a scientifically indefensible exposure surface(s).

The only models where explicit extractable monthly averages will be produced are the IDW estimates. For all others, as specified in the proposal, the investigators when estimating long-term temporal exposures will be using a 5 year average of recent exposure, with the exception of PM2.5 where the 1999-2001or the 2000 periods will be used (to be determined in consultation with ARB staff). The investigators will be estimating long-term temporal exposures with the BME kriging, but had not planned to extract this directly on a monthly basis. However, the investigators have agreed to extract monthly values for the year 2000 and annual values for 1996 – 2000 or 1997– 2001 (period to be determined by consensus with ARB) to conduct model comparison of BME kriging and IDW exposure result estimates. ARB will form a working group comprised of investigators Drs. Jerrett, Christakos, Burnett, Lipsett, Ostro, the ARB staff and others involved in the implementation of the models to determine the best simple exposure model comparison. Health analysis using IDW will ensure that comparability exists between the study titled, "Analyses of Air Pollution and Cardiopulmonary Disease in the California Teachers Study Cohort (Part I & Part II)" and the study titled, "Spatiotemporal

Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort." To the extent practicable and scientifically defensible as defined previously, the Investigators from these two studies will coordinate and collaborate to ensure that the exposure methodologies and health effects assessment in common are equivalent, and to ensure that models used in both of these studies for the association between exposure and health risk are comparable.

All final reports developed under this agreement will be made publicly available on ARB's website. All exposure layers developed within this contract that are scientifically defensible will be assigned to centroids of 2000 census tracts and provided as deliverables to ARB.

Table 1. Total Risk / Replicate LA Study[1] for a California Wide Estimate

MODEL	Year	PM2.5	PM10	O3	NO2	Speciated[2]	Sources[3]	Zipcode	address	w/TC[4]	PM[5]	EDC[6]
IDW(ARBdata)	99-01 or 2000	X						X		X		July 2008
Kriging	99-01 or 2000	X						X				Dec 2008

Table 2. Total Risk / Long Term Temporal Average Exposure California Wide Estimate (A 5yr. Avg. estimate)

MODEL	Year	PM2.5	PM10	O3	NO2	Speciated[2]	Sources[3]	Zipcode	address	w/TC[4]	PM[5]	EDC[6]
IDW(ARBdata)	97-01	X[7]	X	X	X	X			X	X	X	Aug 2009
Kriging	97-01	X[7]	X	X	X	X			X		X	Aug 2009
Kriging w LUR external drift	97-01	X[7]	X	X	X	X			X		X	Aug 2009
Full (BME) Kriging	97-01	X[7]	X	X	X	X			X		X	Aug 2009
NSPE[8]	97-01						X					Aug 2009

Table 3. Total Risk Assessment of Critical Exposure Windows (1982 -2001 or 1988-2001: ARB to supply pollution data from 1982-1988 if possible to extend compilation completed for the Teachers cohort)

MODEL	Year	PM2.5	PM10	O3	NO2	Speciated[2]	Sources[3]	Zipcode	address	w/TC[4]	PM[5]	EDC[6]
IDW(ARBdata)	82-01	X	X	X	X				X	X	X	Nov 2009
Full (BME) Kriging	82-01	X	X	X	X				X		X	Nov 2009

Table 4. Exposure Monthly Model Comparison (2000) and Annual Model Comparison (1996-2000 or 1997 – 2001)												
Note: O3 monthly comparison will include only the months of May – October. NOT November through April.												
MODEL	Mon./Anu.	PM2.5	PM10	O3	NO2	Speciated[2]	Sources[3]	Zipcode	address	w/TC[4]	PM[5]	EDC[6]
IDW(ARBdata)	2000/97-01	X		X					X	X		Dec 2009
Full (BME) Kriging	2000/97-01	X		X					X	X		Dec 2009
ARB staff will form an in house working group to develop with Dr. Jerrett the most appropriate methodology that would best achieve ARB goal of having a meaningful comparison of the various model exposure results within the current budget of this contract. ARB's ultimate goal is to compare all model exposure results via the exposures attributed to the cohort were by each individual in the cohort will be assigned an exposure from each model for PM2.5 and O3.												

Table 5. Sensitivity Analysis: Subset of ACS Mobility Study 15000 subjects (1982-2000)												
MODEL	Year	PM2.5	PM10	O3	NO2	Speciated[2]	Sources[3]	Zipcode	address	w/TC[4]	PM[5]	EDC[6]
IDW(ARBdata)	82-01	X	X	X	X				X			Dec 2009
Full (BME) Kriging	82-01	X	X	X	X				X			Dec 2009

Footnotes for Tables 1 - 5:

1 LA Study: "Spatial Analysis of Air Pollution and Mortality in Los Angeles".
2 Speciated: elemental carbon, organic carbon, metals, nitrates, and sulfates. ARB will be providing the speciated monthly data and IDW surfaces.
3 Sources: Major ports, major highways and road ways, train terminals, airports, etc.
4 w/TC: Will be coordinating and collaborating to the extent practicable with the study titled: "Extended Analyses of Air Pollution and Cardiopulmonary Disease in the California Teachers Study Cohort" to ensure that the exposure methodologies in common are equivalent, and to ensure that the statistical models used for the association of health effects assessment are equivalent in both studies.
5 PM: In addition, this study will investigate the effects from PM coarse if time permits.
6 EDC: Estimated date of Completion can be adjusted based on start date of the contract. These dates are based on starting date June, 07.
7X: The investigators will use for PM25 exposures for 1999-2001 periods for the analysis of Total Risk / Long Term Temporal Average Exposure California Wide Estimate.
8 NSPE: Near Source Proximity Exposure (NSPE) Model.

Example of how to use these tables:

For Table 1.: A California wide total risk will be developed for PM2.5 at the zip code level using the PM2.5 concentrations for the year 2000 or 1999 -2001 replicating the study titled "Spatial Analysis of Air Pollution and Mortality in Los Angeles." Two types of exposure predictions will be developed with the models of IDW and kriging. These exposure predictions will then be analyzed to determine the relative risk for all cause and cause-specific mortalities. The health analysis will be done using the standard Cox model, newly developed Cox-Poisson Random Effects model and Spatial Cohort Survival model. In addition, the investigators will be replicating the analysis above at the address level only for the IDW model and will be coordinating and collaborating to the extent practicable with the study titled: "Extended Analyses of Air Pollution and Cardiopulmonary Disease in the California Teachers Study Cohort" to ensure that the exposure methodologies in common are equivalent, and to ensure that the statistical models used for assessing the association of exposure and health risk are comparable.

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5. Pope, C.A., et al., *Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults.* Am J Resp Critical Care, 1995. **151**: p. 669-674.
6. Lipfert, F.W. and R.E. Wyzga, *Air pollution and mortality: issues and uncertainties.* J Air Waste Manage, 1995. **45**: p. 949-966.
7. Gamble, J.F., *PM2.5 and mortality in long-term prospective cohort studies: Cause-effect or statistical associations?* Environ Health Perspect, 1998. **106**: p. 535-549.
8. HEI, *Assessing Health Impact of Air Quality Regulations: Concepts and Methods for Accountability Research. Health Effects Institute.* 2003: Boston, MA.
9. Krewski, D., et al., *Overview of the reanalysis of the Harvard Six Cities study and American Cancer Society study of particulate air pollution and mortality. J Toxicol Environ Health A 66:1507-1552.* J Toxicol Environ Health A, 2003. **66**: p. 1507-1552.
10. Jerrett, M., et al., *Spatial analysis of the air pollution-mortality relationship in the context of ecologic confounders.* J Toxicol Env Health, 2003. **66**: p. 1735-1777.
11. Hoek, G., et al., *Association between mortality and indicators of traffic-related air pollution in The Netherlands: a cohort study.* Lancet, 2002. **360**: p. 1203-1209.
12. Nafstad, P., et al., *Urban air pollution and mortality in a cohort of Norwegian men.* Environ Health Persp, 2004. **112**: p. 610-615.
13. Kunzli, N., et al., *Ambient air pollution and atherosclerosis in Los Angeles.* Environ Health Persp, 2005. **113**: p. 201-206.
14. Nafstad, P., et al., *Lung cancer and air pollution: a 27 year follow up of 16 209 Norwegian men.* 2003. **58**: p. 1071-1076.
15. Goddard, M.J., D.J. Murdoch, and D. Krewski, *Temporal aspects of risk characterization.* Inhal Toxicol, 1995. **7**: p. 1005-1018.
16. Zeger, S.L., F. Dominici, and J.M. Samet, *Harvesting-resistant estimates of air pollution effects on mortality.* Epidemiol, 1999. **10**: p. 171-175.
17. Schwartz, J., *Harvesting and long term exposure effects in the relation between air pollution and mortality.* Am J Epidemiol, 2000. **151**: p. 440-448.
18. Brunekreef, B., *Air pollution and life expectancy: is there a relation?* Occup Environ Med, 1997. **54**: p. 781-784.

19. Goldberg, M.S., et al., *Identifying subgroups of the general population that may be susceptible to short-term increases in particulate air pollution: A time series study in Montreal, Quebec. Health Effects Institute, Number 97, Cambridge, MA.* 2000, Hansen KA: Cambridge, MA.
20. Goldberg, M.S., et al., *The association between daily mortality and short-term effects of ambient air particulate pollution in Montreal, Quebec: 1. Nonaccidental mortality.* Environ Res, 2001. **86**: p. 12-25.
21. Goldberg, M.S., et al., *The association between daily mortality and short-term effects of ambient air particle pollution in Montreal, Quebec: 2. Cause-specific mortality.* Environ Res, 2001. **86**: p. 26-36.
22. Krewski, D., et al., *Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality, Part II: Sensitivity Analysis : A Special Report of the Institute's Particle Epidemiology Reanalysis Project. Health Effects Institute, Cambridge, MA.* 2000: Cambridge, MA. p. 129-240.
23. Villeneuve, P.J., et al., *Fine particulate air pollution and all-cause mortality with the Harvard Six-cities Study: Variations in risk by period of exposure.* Ann Epidemiol, 2002. **12**: p. 568-576.
24. Jerrett, M., et al., *Geographies of uncertainty in the health benefits of air quality improvements.* Journal Submitted, 2006.
25. Laden, F., et al., *Reduction in fine particulate air pollution and mortality: extended follow-up of the Harvard Six Cities study.* Am J Resp Crit Care, 2006. **173**: p. 667-672.
26. O'Neil, M., et al., *Health, wealth and air pollution.* Environ Health Persp, 2003. **111**: p. 186-187.
27. Kwan, M.P. and L. J., *Geovisualization of human activity patterns using 3D GIS: a time-geographic approach*, in *Spatially Integrated Social Science: Examples in Best Practice*, G. M.F. and J. D.G., Editors. 2004, Oxford University Press: New York. p. 48-66.
28. Jerrett, M., et al., *A review and evaluation of intraurban air pollution exposure models.* J Expo Anal Env Epid, 2005. **15**: p. 185-204.
29. Ross, Z., et al., *Nitrogen dioxide prediction in southern California using land use regression modeling: potential for environmental health analyses.* . J Expo Anal Env Epid, 2006. **16**: p. 106-114.
30. Jerrett, M., et al., *Modelling the intra-urban variability of ambient traffic pollution in Toronto, Canada.* Journal of Toxicology and Environmental Health, 2006. **In Press**(NERAM - Special Issue).
31. Kanaroglou, P., et al., *Establishing an air pollution monitoring network for intra-urban population exposure assessment: A location-allocation approach.* Atmospheric Environment, 2005. **39**(13): p. 2399-2409.
32. Sahsuvaroglu, T., et al., *A land use regression model for predicting ambient concentrations of nitrogen dioxide in Hamilton, Ontario, Canada.* Journal of Air Waste Management Association, 2006. **56**(8): p. 1059-1069.

33. Gilbert, N.L., et al., *Assessing spatial variability of ambient nitrogen dioxide in Montreal, Canada, with a land-use regression model.* J Air Waste Man, 2005. **55**: p. 1059-1063.
34. Moore, D.K., et al., *A land use regression model for predicting ambient fine particulate matter across Los Angeles, CA.* Journal of Environmental Modelling, 2006. **submitted.**
35. English, P., et al., *A land use regression for predicting traffic pollution in Alameda County.* 2006(in preparation).
36. Chen, H., et al., *Land use regression models for traffic pollution with temporally discordant monitoring data.* 2006(in preparation).
37. Ross, Z., et al., *A land use regression model for predicting fine particulate matter concentrations in the New York City region.* 2006.
38. Henderson, S.B., et al., *Application of land use regression to estimate ambient concentration of traffic-related NOx and fine particulate matter.* Environmental Science and Technology, 2006. **Accepted for Publication.**
39. Christakos, G., *On certain classes of spatiotemporal random fields with application to space-time data processing.* IEEE Trans Systems, Man, and Cybernetics, 1991. **21**(4): p. 861-875.
40. Burrough, P.A. and R.A. McDonnell, *Principals of Geographical Information Systems.* 1998, Oxford: Oxford University Press.
41. Christakos, G. and D.T. Hristopulos, *Spatiotemporal Environmental Health Modelling.* 1998, Boston, MA: Kluewer Academic Publication.
42. Christakos, G., et al., *Interdisciplinary Public Health Reasoning and Epidemic Modelling: The Case of Black Death.* 2005, New York, NY: Springer-Verlag.
43. Christakos, G. and M.L. Serre, *A spatiotemporal study of exposure-health effect associations.* Journal of Exposure Analysis and Environmental Epidemiology, 2000. **10**(2): p. 168-187.
44. Christakos, G., P. Bogaert, and M.L. Serre, *Temporal GIS.* (with CD-ROM) ed. 2002, New York, NY: Springer-Verlag.
45. Yu, H.L., et al., *Interactive Spatiotemporal Modelling of Health Systems: The SEKS-GUI Framework.* SERRA Special Issue on Medical Geography as a Science of Interdisciplinary Knowledge Synthesis under Conditions of Uncertainty, 2006.
46. Christakos, G., *Random Field Models in Earth Sciences.* New Edition ed, ed. S.D. Academic Press. 1992, Mineola, NY: Dover Publications Inc.
47. Ma, R., D. Krewski, and R.T. Burnett, *Random effects Cox models: A Poisson modelling approach.* Biometrika, 2003. **90**: p. 157-169.
48. Therneau, T.M., Grambsch,P.M., *Modelling Survival Data.* 2000, New York, NY: Springer-Verlag.
49. Andersen, P.K. and R.D. Gill, *Cox's regression model for counting processes: a large sample study.* Ann Stat, 1982. **10**: p. 1100-1120.
50. Whitehead, J., *Fitting Cox's regression model to survival data using GLIM.* Appl Statist, 1980. **29**: p. 268-275.
51. Hughes, E., *Alogorithmic Description of the Cox-Poisson Program - Technical Report included with the Cox-Poisson Distribution Package.* 2006.

CV OF THE INVESTIGATORS

Principal Investigator/Program Director (Last, First, Middle):

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Jerrett, Michael L.B.	Associate Professor
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Trent University	B.Sc.	1986	Environment Resource
University of Toronto	M.A.	1988	Political Science
University of Toronto	Ph.D.	1996	Geography
McMaster University	Postdoc.	9/95 –4/97	Environmental Health

A. Positions and Honors

Positions and Employment

1989-1991 Environmental Planner, Land Use Planning Unit, Environmental Planning Section, Approvals Branch, Ontario Ministry of the Environment
1995-1997 Postdoctoral Fellow, Geography and Geology Department, McMaster University
1997-1998 Assistant Professor, Geography Department, San Diego State University
1998-2003 Associate Professor (promoted from Assistant in 2002), School of Geography and Geology, and Health Studies Program, McMaster University
2003-Present Associate Professor, Preventive Medicine Department, Keck School of Medicine, University of Southern California
2006-Present Associate Professor, Division of Environmental Health Sciences, School of Public Health, University of California, Berkeley

Other Experiences and Professional Memberships

Member Association of American Geographers
Member International Society for Exposure Analysis
2001-2003 Canadian Institutes of Health Research Population Health Review Committee
1998-Present U.S. National Science Foundation (Reviewer)
2005-06 U.S. National Institute of Environmental Health Science Special Review Panel Member

Honors

2003 Dangermond Endow Speaker in Geographic Information Science, Environmental Systems Research Institute, Redlands, CA and University of California, Santa Barbara
1998 Nystrom Award Competition Finalist, Association of American Geographers (USA).
1997 Certificate of Excellence, Undergraduate Teaching Award, Student Union of McMaster University.
1995 Teaching Postdoctoral Fellowship, Tri-Council Research, MIEH, McMaster University.

B. Selected peer-reviewed publications (in chronological order)

1. Jerrett, M., J. Eyles, D. Cole, and S. Reader Environmental equity in Canada: An empirical investigation into the income distribution of pollution in Ontario. Environment and Planning A 29: 1777-1800, 1997.
2. Jerrett, M.Green costs, red ink: Determinants of municipal defensive expenditures. The Professional Geographer 51:115-134, 1999.
3. Jerrett, M., J. Eyles, and D. Cole. Socioeconomic and environmental covariates of premature mortality in Ontario. Social Science and Medicine 47: 33-49, 1998.
4. Luginaah, I, M. Jerrett, S. Elliott, J. Eyles, K. Parizeau, S. Birch, B. Hutchinson, G. Veestra, C. Giovis.

C. Research Support

Ongoing Research Support

5 P30 ES07048-10 (Peters) 04/01/96 – 03/31/06
NIEHS
Environmental Exposures, Host Factors and Human Disease
Specific aims of project: Multidisciplinary center for research aimed at identifying and characterizing (1) the direct human health effects of environmental exposures and (2) factors which modify susceptibility to environmental exposures, including genetic factors and interactions with other environmental exposures, such as diet.

5 P01 ES11627-04 (Peters) 07/01/02 – 06/30/07
NIEHS
Genetics, Air Pollution, and Respiratory Effects in Children and Young Adults
Specific aims of project: Building on the existing Children's Health Study, an on-going cohort of 6000 children, the four projects under this program project will address the question of whether the observed changes in pulmonary function persist to adulthood; involve studying asthma incidence with the goal of identifying host factors; examine the genetic variation in oxidative stress pathways that modulate response to air pollution, and develop new biostatistical methods.

Canadian Institutes of Health Research (Jerrett) 10/01/03 – 10/31/07
Specific aims of project: A cohort study of mortality in relation to intra-urban air pollution variability and traffic exposure.

G3K10394 EPA-2003STAR K-1 (Jerrett) 10/01/04 – 09/30/07
Spatial Exposure Models for Assessing the Relationship Between
Air Pollution and Childhood Asthma at the Intra-Urban Scale
Specific aims of project: To derive new estimates of ambient air pollution concentration and potential exposures in a large population of children of Los Angeles County (utilizing an existing cohort of the Children's Health Study) in order to illustrate the importance of exposure uncertainty to health effects assessment The within-community risk assessment will emphasize areas of highest risk, potentially leading to more equitable and efficient air pollution policies.

1 R03 ES014046-01 (Jerrett)
National Institute of Environmental Health Sciences 07/01/05 – 06/30/10
Socioeconomic Status, Stress, Air Pollution and Asthma

Primary Specific Aims: (1) Refining and applying new statistical methods for multilevel modeling of social characteristics that may explain the differences between communities in the incidence of wheeze and ultimately of asthma; (2) Examining the role of stress as an explanation for any observed relationships between contextual social characteristics and wheeze; (3) Assessing confounding and effect modification of the relationship between air pollution and incident wheeze in the ongoing CHS studies.

1 U54 CA116848-01 (Goran)
National Institutes of Health 09/01/05 – 08/31/10
Influence of Built Environments on the Development
of Obesity During Childhood

Primary Specific Aims (Project 3, Jerrett PI): (1) To assess the association between the built environment and obesogenic trajectories during childhood growth and development; and (2) to examine whether individual (i.e., race, SES) and contextual variables (i.e., air pollution) modify the association between the built environment and obesogenic trajectories.

Neighborhood Predictors of Class I Urban Trail Use (Reynolds)

Traffic Pollution and Children's Health: Refining Estimates of Exposure for the East Bay Children's Health Study (Jerrett) 10/01/05 – 10/01/07

Land Use Regression Models for Traffic-Related Air Pollution and Asthma in Economically Disadvantaged and High Traffic Density Neighborhoods in Los Angeles County, California (Jerrett) 10/01/05 – 10/01/07

CURRICULUM VITAE

George Christakos, Ph.D, DSc, PE

Department of Geography

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5500 Campanile Drive

San Diego, CA 92182-4493, USA

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FACULTY POSITIONS

2006-Present:

Department of Geography,
San Diego State University, San Diego, California, USA:

- *Birch Distinguished Professor*.

Teaching and research activities focus on the advanced modelling and space-time mapping of interdisciplinary natural systems, including: Multi-scaled environmental processes; Integrated temporal geographical information systems; Cognitive techniques of multi-sourced knowledge synthesis and data assimilation; Interdisciplinary human exposure analysis and health effects; Model-based risk assessment and decision making; Medical geography, epidemiology, and the space-time propagation of infectious diseases; Random field models and spatiotemporal statistics; Fluid mechanics, contaminant flow and transport; Air pollution monitoring and control.

1990-2005:

Department of Environmental Science & Engineering,

School of Public Health,
University of North Carolina, Chapel Hill, N.C., USA:

- 1998-Present: *Professor*.
- 1999-2005: *Director*, Center for the Integrated Study of the Environment (CISE).

- 1999-2002: *Director*, Environmental Modelling (EM) program.
- 1994-1997: *Associate Professor*.
- 1990-1993: *Assistant Professor*.

2001-2005:
Department of Statistics & Operations Research
University of North Carolina, Chapel Hill, N.C., USA:

Adjunct Professor

OTHER APPOINTMENTS

May, 2003: Unite d'Environnemetrie at de Geomatique, Universite Catholique de Louvain-la-Neuve, Louvain la Neuve, Belgium: *Visiting Professor*.

January-April, 2003: Environmental Laboratory, National Technical University of Athens, Athens, Greece: *Visiting Scholar*.

November-December 2001 & April 11-22, 2002: Departments of Engineering & Applied Mathematics, Universidad Politecnica de Catalunya, Barcelona, Spain, and Department of Statistics, Universidad de Granada, Granada, Spain: *Visiting Professor*.

October 2001: Dipartimento di Scienze Economiche e Matematico-Statistiche, Universita' di Lecce, Lecce, Italy: *Visiting Professor*.

September 2001: Russian Academy of Sciences, Nuclear Safety Institute, Moscow, Russia: *Visiting Professor*.

1993-1994: Department of Geological & Environmental Sciences, Stanford University, Stanford, CA, USA, and Department of Petroleum Engineering, Stanford University, Stanford, CA, USA: *Visiting Faculty*.

1988-1990: Division of Applied Sciences, Harvard University, Cambridge, MA, USA: *PhD Fellow*.

1987:
Department of Applied Mathematics & Theoretical Physics, University of Cambridge, Cambridge, UK: *Visiting Research Fellow*.

1986 and 1988: Advanced Projects Section, Kansas Geological Survey, Lawrence, KS, USA: *Visiting Research Fellow*.

1985-1986: Institute of Geology & Mineral Exploration, Athens, and National Technical University of Athens, Greece: *Research Associate*.

1982-1983:
Centre de Geostatistique et de Morphologie Mathematique,, Ecole des Mines de Paris, Fontainebleau, France: *Research Associate*.

1980-1982: Department of Civil Engineering, Massachusetts Institute of Technology, Cambridge, MA, USA: *MS Research Assistant*.

1979-1980: Soil Mechanics Laboratory, University of Birmingham, Birmingham, UK: *MS Laboratory Research Assistant*.

EDITORIAL POSITIONS

1998-Present: *Journal of Stochastic Environmental Research & Risk Assessment*.
Editor-in-Chief

1992-Present: *Journal of Environmental & Ecological Statistics*.
Editorial Group

1997-Present: *Advances in Water Resources*.
Editorial Board

1994-1997: *Journal of Stochastic Hydrology & Hydraulics*.
Associate Editor

FOREIGN LANGUAGES

- *Greek* (Greek-born USA citizen)
- *French* (Dipl. Univ. de Besancon)
- *German* (Grundst. Dipl.)

PUBLIC DOMAIN COMPUTER LIBRARIES

- BMElib (Bayesian Maximum Entropy software library).

- SANlib (Stochastic Analysis software library).
- SEKS-GUI (Spatiotemporal Epistematics Knowledge Synthesis-Graphic User Interface)

SCIENTIFIC PUBLICATIONS

I. Books:

Christakos, G., R.A. Olea, M.L. Serre, H.L. Yu, and L-L. Wang: *Interdisciplinary Public Health Reasoning and Epidemic Modelling: The Case of Black Death.* Springer-Verlag, New York, N.Y., 319 p., 2005.

Christakos, G., P. Bogaert and M.L. Serre: *Temporal GIS.* Springer-Verlag, New York, NY, 220 p., With CD-ROM, 2002.

Christakos, G.: *Modern Spatiotemporal Geostatistics.* Oxford Univ. Press, New York, NY, 304 p., 2000.

Christakos, G. and D.T. Hristopulos: *Spatiotemporal Environmental Health Modelling: A Tractatus Stochasticus.* Kluwer Academic Publ., Boston, MA, 423 p., 1998.

Christakos, G.: *Random Field Models in Earth Sciences.* Academic Press, San Diego, CA, 474 p., 1992. (Out of Print.)

Christakos, G.: *Random Field Models in Earth Sciences. New* edition, Dover Publ. Inc., Mineola, NY, 2005.

Christakos, G., I. Clark, M. David, A.G. Journel, D.G. Krige and R.A. Olea: *Geostatistical Glossary & Multilingual Dictionary*: Oxford Univ. Press, Oxford, UK, 177 p., 1991.

II. Contributions in Encyclopedias:

Christakos, G. "Stochastic Modelling of Human Exposure". In *Encyclopedia of Enviromentrics*, A. H. El-Shaarawi & W.W. Piegorsch (eds.), Vol. 3, 1290-1296, J. Wiley & Sons, Ltd., Chichester, U.K., 2001.

Christakos, G. "The Study of Uncertainty in Life Support Systems". In *Encyclopedia of Life Support Systems*. UNESCO, [http://www.eolss.net/], London, UK, 2004.

III. Papers in Refereed Journals:

Public Health:

Choi, K-M, G. Christakos and M.L. Wilson, "El Niño effects on influenza mortality Risks in the State of California". Vol. 120, pp. 505-516, 2006.

Christakos, G., R.A. Olea and H-L Yu, "Recent results on the spatiotemporal modelling and comparative analysis of Black Death and Bubonic Plague epidemics". Submitted, 2006.

Environmental Science & Technology:

Christakos, G., "Critical conceptualism in environmental modelling and prediction". Vol. 37, pp. 4685-4693, 2003.

Risk Analysis:

Serre, M.L., A. Kolovos, G. Christakos and K. Modis, "An application of the holistochastic human exposure methodology to naturally occurring Arsenic in Bangladesh drinking water". Vol. 23(3), pp. 515-528, 2003.

International Journal of Health Geographics:

Yu H-L and G. Christakos "Spatiotemporal Modelling and Mapping of the Bubonic Plague Epidemic in India". Vol. 5(12), 2006. Highly-accessed paper.

Jour. of Exposure Analysis & Environmental Epidemiology:

Christakos, G. and A. Kolovos, "A study of the spatiotemporal health impacts of ozone exposure". Vol. 9(4), pp. 322-335, 1999.

Christakos, G. and M.L. Serre, "A spatiotemporal study of exposure-health effect associations". Vol. 10(2), pp. 168-187, 2000.

Choi, K-M, M. L. Serre, and G. Christakos. "Efficient mapping of California mortality fields at different spatial scales". Vol. 13(2), pp. 120-133, 2003.

Yu, H-L, J-C Chen and G. Christakos, 2006. "BME space-time mapping of residential level ambient PM10 and Ozone exposures at multi-temporal scales in the states of North and South Carolina". Submitted, 2006.

Social Science & Medicine D: Medical Geography:

Christakos, G. and J. Lai, "A study of the breast cancer dynamics in North Carolina". Vol. 45(10), pp. 1503-1517, 1997.

Christakos, G. and V. Vyas, "A novel method for studying population health impacts of spatiotemporal ozone distribution". Vol. 47(8), pp. 1051-1066, 1998.

Human Biology:

Olea, R.A. and G. Christakos, "Duration of urban mortality for the 14th century Black Death epidemic". Vol. 77(3), 291-303, 2005.

Jour. of Sexually Transmitted Infections:

Law, D.G., M.L. Serre, G. Christakos, P.A. Leone and W.C Miller, "Spatial analysis and mapping of sexually transmitted diseases to optimize intervention and prevention strategies". Vol. 80, pp. 294-299, 2004.

Geoderma:

Christakos, G., "Spatiotemporal information systems in soil and environmental sciences". Vol. 85(2-3), pp. 141-179, 1998.

Savelieva, E, V. Demyanov, M. Kanevski, M.L. Serre, and G. Christakos, "BME-based uncertainty assessment of the Chernobyl fallout". Vol. 128, pp. 312-324, 2005.

Reviews of Geophysics:

Christakos, G., "Recent methodological developments in geophysical assimilation modelling". Vol. 43, pp. 1-10, 2005.

Jour. of Geophysical Research:

Bogaert, P. and G. Christakos, "Spatiotemporal analysis and processing of thermometric data over Belgium". Vol. 102(D22), pp. 25,831-25,846, 1997.

Christakos, G., M.L. Serre and J. Kovitz, "BME representation of particulate matter distributions in the state of California on the basis of uncertain measurements". Vol. 106(D9), pp. 9717-9731, 2001.

Water Resources Research:

Christakos, G., "On the problem of permissible covariance and variogram models". Vol. 20(2), pp. 251-265, 1984.

Christakos, G. and B.R. Killam, "Sampling design for classifying contaminant level using annealing search algorithms". Vol. 29(12), pp. 4063-4076, 1993.

Christakos, G. D.T. Hristopoulos, and C.T. Miller, "Stochastic diagrammatic analysis of groundwater flow in heterogeneous soils". Vol. 31(7), pp. 1687-1703, 1995.

Christakos, G. and D.T. Hristopulos, "Stochastic indicators for waste site characterization". Vol. 32(8), pp. 2563-2578, 1996.

Christakos, G., D.T. Hristopulos and X. Li, "Multiphase flow in heterogeneous porous media: A stochastic differential geometry viewpoint". Vol. 34(1), pp. 93-102, 1998.

Kolovos, A., G. Christakos, M.L. Serre and C.T. Miller, "Computational BME solution of a stochastic advection-reaction equation in the light of site-specific information". Vol. 38(12), pp. 1318-1334, 2002.

Yu, H-L, K. Modis, G. Papantonopoulos and G. Christakos, 2006. "BME Solution of a Stochastic Physical Equation Representing a Three-Dimensional Geothermal Field in Nea Kessiani, Greece". Submitted. 2006.

Stochastic Hydrolology & Hydraulics:

Christakos, G., C.T. Miller, and D. Oliver, "The development of stochastic space transformation and diagrammatic perturbation techniques in subsurface hydrology". Vol. 7(1), pp. 14-32, 1993.

Christakos, G., C.T. Miller and D. Oliver , "Stochastic perturbation analysis of ground water flow. Spatially variable soils, semi-infinite domains and large fluctuations". Vol. 7(3), pp. 213-239, 1993.

Oliver, L.D., and G. Christakos, "Diagrammatic solutions for hydraulic head moments in 1-D and 2-D Bounded domains". Vol. 9, pp. 269-296, 1995.

Christakos, G. and D.T. Hristopulos, "Stochastic space transformation techniques in subsurface hydrology-Part 2: Generalized spectral decompositions and Plancherel representations". Vol. 8(2), pp. 117-155, 1994.

Hristopulos D. T. and G. Christakos, "Diagrammatic theory of nonlocal effective hydraulic conductivity". Vol. 11(5), pp. 369-395, 1997.

Bogaert, P. and G. Christakos, "Stochastic analysis of spatiotemporal solute content measurements using a regressive model". Vol. 1(4), pp. 267-295, 1997.

Advances in Water Resources:

Christakos, G., "Space transformations in the study of multidimensional functions in the hydrologic sciences". Vol. 9(1), pp. 42-48, 1986.

Christakos, G. and R.A. Olea, "Sampling design for spatially distributed hydrogeologic and environmental processes". Vol. 15(4), pp. 219-237, 1992.

Oliver, L.D., and G. Christakos, "Boundary condition sensitivity analysis of the stochastic flow equation". Vol. 19(2), pp. 109-120, 1996.

Miller, C.T., G. Christakos, P.T. Imhoff, J.F. McBride, J.A. Pedit, and J.A. Trangenstein, "Multiphase flow and transport modelling in heterogeneous porous media: Challenges and approaches". Vol. 21(2), pp. 77-120, 1998.

Christakos, G., D.T. Hristopulos and P. Bogaert, "On the physical geometry hypotheses at the basis of spatiotemporal analysis of hydrologic geostatistics". Vol. 23, pp. 799-810, 2000.

Christakos, G., "On the assimilation of uncertain physical knowledge bases: Bayesian and non-Bayesian techniques". Vol. 25(8-12), pp. 1257-1274, 2002.

Kolovos, A., G. Christakos, D.T. Hristopulos and M.L. Serre, "Methods for generating non-separable spatiotemporal covariance models with potential environmental applications". Vol. 27, pp. 815-830, 2004.

Physical Review E:

Hristopoulos, D.T. and G. Christakos, "A variational calculation of the effective fluid permeability of heterogeneous media". Vol. 55(6), pp. 7288-7298, 1997.

Bulletin of American Physical Society:

Hristopulos, D.T. and G. Christakos, "Monte Carlo calculations of single-phase effective permeability in 2-D anisotropic porous media". Vol. 44(6), p. 23, 1999.

Atmospheric Environment:

Christakos, G. and G.A. Thesing, "The intrinsic random field model and its application in the study of sulfate deposition data". Vol. 27A(10), pp. 1521-1540, 1993.

Christakos, G. and D.T. Hristopulos: "Characterization of atmospheric pollution using stochastic indicators". Vol. 30(22), pp. 3811-3823, 1996.

Vyas, V. and G. Christakos, "Spatiotemporal analysis and mapping of sulfate deposition data over the conterminous USA". Vol. 31(21), pp. 3623-3633, 1997.

Christakos, G. and V. Vyas "A composite spatiotemporal study of ozone distribution over Eastern United States". Vol. 32(16), pp. 2845-2857, 1998.

Christakos, G. and M.L. Serre, "BME analysis of spatiotemporal particulate matter distributions in North Carolina". Vol. 34(20), pp. 3393-3406, 2000.

Nonlinear Analysis:

Hristopulos, D.T. and G. Christakos, "An analysis of hydraulic conductivity upscaling". Vol. 30(8), pp. 4979-4984, 1997.

Institute of Electrical & Electronic Engineers (IEEE) Transactions:

Christakos, G., "On certain classes of spatiotemporal random fields with application to space-time data processing". *Systems, Man, and Cybernetics*. Vol. 21(4), pp. 861-875, 1991.

Christakos, G. and C. Panagopoulos, "Space transformation methods in the representation of geophysical random fields". *Geosciences and Remote Sensing*. Vol. 30(1), pp. 55-70, 1992.

Christakos, G. and P. Bogaert, "Spatiotemporal analysis of springwater ion processes derived from measurements at the Dyle Basin in Belgium". *Geosciences and Remote Sensing*. Vol. 34(3), pp. 626-642, 1996.

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Yu, H-L, and G. Christakos, "Dealing with Spatiotemporal Heterogeneity: The Stochastic BME-v/μ Model". Submitted, 2005.

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Hristopoulos, D.T., G. Christakos, and M. Serre, "Implementation of a space transformation approach for solving the three-dimensional flow equation". *SIAM-Scientific Computing.* Vol. 20(2), pp. 619-647, 1999.

Christakos, G., D.T. Hristopulos and A. Kolovos, "Stochastic flowpath analysis of multiphase flow in random porous media". *SIAM-Applied Mathematics.* Vol. 60(5), pp. 1520-1542, 2000.

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Jour. of Optimization Theory & Applications:

Christakos, G. and P.N. Paraskevopoulos, "On the functional optimization of a certain class of nonstationary spatial functions". Vol. 52(2), pp. 191-208, 1987.

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Jour. of Applied Probability:

Christakos, G. and D. T. Hristopulos, "Stochastic indicator analysis of contaminated sites". Vol. 34(4), pp. 988-1008, 1997.

Stochastic Environmental Research & Risk Assessment:

Serre, M.L. and G. Christakos, "Modern Geostatistics: Computational BME in the light of uncertain physical knowledge -The Equus Beds study". Vol. 13(1), pp. 1-26, 1999.

Hristopulos, D.T. and G. Christakos, "Renormalization group analysis of permeability upscaling". Vol. 13(2), pp. 131-160, 1999.

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Christakos, G., "Stochastic simulation of spatially correlated geoprocesses". Vol. 19(8), pp. 803-827, 1987.

Christakos, G., "On-line estimation of nonlinear physical systems". Vol. 20(2), pp. 111-133, 1988.

Christakos, G., "A Bayesian/maximum-entropy view to the spatial estimation problem". Vol. 22(7), pp. 763-776, 1990.

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Engineering Geology:

Christakos, G., "Modern statistical analysis and optimal estimation of geotechnical data". Vol. 22(2), pp. 175-200, 1985.

Jour. of Mathematical & Computer Modelling:

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Christakos, G. and R.A. Olea, "A multiple-objective optimal exploration strategy". Vol. 11, 413-418, 1988.

IV. Papers in Refereed Volumes:

Geostatistics for Environmental Applications:

Serre, M., G. Christakos, J. Howes and A.G. Abdel-Rehiem, "Powering an Egyptian air quality information system with the BME space/time analysis toolbox: Results from the Cairo baseline year study". Monestiez, P., D. Allard and R. Froidevaux (eds.), pp. 91-100, Kluwer Acad. Publ., Dordrecht, the Netherlands, 2001.

Christakos, G., M.G. Serre, V. Demyanov, M. Kanevski, E. Savelieva, S. Chernov and V. Timonin, "BME analysis of neural network residual data from the Chernobyl fallout: Bayesian and non-Bayesian approaches". Monestiez, P., D. Allard and R. Froidevaux (eds), pp. 509-510, Kluwer Acad. Publ., Dordrecht, the Netherlands, 2001.

Christakos, G., "Global BME mapping of ozone distribution by assimilating soft information and data from TOMS and SBUV instruments on the Nimbus 7 satellite". In *geoENV IV*, Sanchez-Vila, X. and J. Carrera (editors), Kluwer Academic Publishers, Dordrecht, The Netherlands, 2004.

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Spatiotemporal Modelling of Environmental Processes:

Christakos, G., "Integrated modelling in space-time environments: A synthetic theory of human exposure". Invited paper, METMA'04, Granada, Spain; In press, 2005.

Fundamental Theories of Physics:

Christakos, G., "Some applications of the Bayesian maximum entropy concept in geostatistics". Invited paper, Kluver Acad. Publ., pp. 215-229, Amsterdam, The Netherlands, 1990.

Modelling and Simulation of Systems:

Christakos, G., "Modelling and estimation of nonlinear systems". *IMAC,* Baltzer AG Sci. Publ., pp. 221-223, 1989.

Civil Engineering & Computers:

Christakos, G. and R. Dimitrakopoulos, "Developing intelligent computer models in the stochastic analysis of environmental systems", pp. 213-218, Oxford, UK, 1991.

Geostatistics for the Next Century:

Christakos, G., C.T. Miller, and D. Oliver, "Cleopatra's nose and the diagrammatic approach to flow modelling in random porous media". Kluver Acad. Publ., pp. 341-358, Amsterdam, The Netherlands, 1993.

Probabilistic & Stochastic:

Christakos, G., "Certain results on spatiotemporal random fields and their applications in environmental research". Vol. 372, pp. 287-322, 1992.

Calibration and Reliability in Groundwater Modelling: A Few Steps Closer to Reality:

Christakos, G., "The role of conceptual frameworks in hydrologic research and development". K. Kovar and Z. Hrkal (eds.), IAHS Publ. 277, Oxfordshire, U.K., pp. 277- 285, 2003.

Serre, M.L. and G. Christakos. "Efficient BME estimation of subsurface hydraulic properties using measurements of water table elevation in unidirectional flow". K. Kovar and Z. Hrkal (eds.), IAHS Publications No. 277, Oxfordshire, UK, pp. 321-327, 2003.

Computational Methods in Surface & Groundwater Transport:

Christakos, G., "Multi-point BME space/time mapping of environmental variables". Burganos, V.N., G.P. Karatzas, A.C. Payatakes, W.G. Gray & G.F. Pinder (eds.),

Vol. 2, pp. 289-296, Computational Mechanics Publications, Southampton, UK, 1998.

V. Papers in Refereed Conference/Symposia Proceedings:

ModelCARE2002:

Serre, M.L. and G. Christakos, "BME-based hydrogeologic parameter estimation in groundwater flow modelling". IAHS Proc., pp. 566-570, Prague, Czech Republic, June 17-20, 2002.

Christakos, G., "Conceptual framework of physical knowledge synthesis in uncertain environments". Keynote talk, IAHS Proc., pp. 535-539, Prague, Czech Republic, June 17-20, 2002.

GeoEnv2000:

Demyanov, V., M.L. Serre, G. Christakos, V. Timonin, V., M. Kanevski, E. Savelieva, and S. Chernov, "Neural network residual BME analysis of Chernobyl fallout-Part II". *Third European Conference on Geostatistics for Environmental Applications*, Vol. 1, pp. 99-110, Nov. 22-24, 2000, Avignon, France, 2000.

Joint Intern. Symposium on Geospatial Theory, Processing & Applications

Choi, K-M, G. Christakos and M.L. Wilson. "A new multi-scale modelling approach for space/time random field estimation", Ottawa, Canada, July 9-12, 2002.

Air Pollution 2002:

Christakos, G., A. Kolovos and M.L. Serre, C. Abhichek and F. Vukovich, "Towards global mapping of ozone distribution using soft information and data from TOMS and SBUV instruments on the Nimbus-7 satellite", Segovia, Spain, July 1-3, 2002.

Serre, M.L. and G. Christakos, "Efficient exposure mapping across space-time of particulate matter in the US", Segovia, Spain, July 1-3, 2002.

Pedometrics 2003:

Savelieva, E., V. Demyanov, M. Kanevski, M.L. Serre and G. Christakos, "BME application for uncertainty assessment of the Chernobyl fallout", 5th Conf. of the

Provisional Commission on Pedometrics of the Intern. Union of Soil Sciences, Reading, U.K., September 2003.

IEEE Symposia:

Christakos, G., C.T. Miller, and D. Oliver, "Stochastic flow modelling in terms of interactive perturbation, Feynman diagrams and graph theory". In Proceed of *Southeastcon-93*, 77-84, April 4-7, 1993.

Christakos, G., Kolovos, A., Serre, M.L., and Vukovich, F.M., "Generating high spatial resolution analyses of SBUV stratospheric ozone for calculating the tropospheric ozone residual (TOR)". In Proceed of *Intern. Geoscience & Remote Sensing Symposium* (IGARSS2003), Toulouse, France, 21-25 July, 2003.

Modelling and Simulation:

Christakos, G., "The space transformations and their applications in systems modelling and simulation". *12th Intern. Confer.*, AMSE, Vol. 1(3), pp. 49-68, Athens, Greece, 1984.

METMA'04:

Christakos, G., " Integrated modelling in space-time environments: Toward a synthetic theory of human exposure ". 2nd Spanish Workshop on Spatio-Temporal Modelling of Environmental Processes (METMA'04), Granada, Spain, June 1-4, 2004.

International Statistical Institute:

Choi, K-M, M. L. Serre, and G. Christakos. "Space/time BME analysis and mapping of mortality in California". 53rd Session, Seoul, S. Korea, 22-29 August, 2001.

Computational Methods in Water Resources (CMWR):

Christakos, G., " The cognitive basis of physical modelling". Proceed. CMWR04, Chapel Hill, NC, USA, June 13-17, 2004.

International Association for Mathematical Geology:

Bogaert P. and G. Christakos, "Stochastic analysis of space/time processes using a multicomponent regressive model". *4th Annual Conference* - Vol. 1, Buccianti A., G. Nardi, and R. Potenza (eds.), pp. 85-90, De Frede Editore, Naples, Italy, 1998.

Serre, M.L., P. Bogaert and G. Christakos, "Computational investigations of Bayesian maximum entropy spatiotemporal mapping". *4th Annual Conference* - Vol.1, Buccianti A., G. Nardi, and R. Potenza (eds.), pp. 117-122, De Frede Editore, Naples, Italy, 1998.

Choi, K-M., G. Christakos, and M.L. Serre, "Recent developments in vectorial and multi-point BME analysis". *4th Annual Conference* -Vol. 1, Buccianti A., G. Nardi, and R. Potenza (eds.), pp. 91-96, De Frede Editore, Naples, Italy, 1998.

Christakos, G., "While God is raining brains, are we holding umbrellas? The role of Modern Geostatistics in spatiotemporal analysis and mapping." Keynote lecture. *4th Annual Conference* - Vol. 1, Buccianti A., G. Nardi, and R. Potenza (eds.), pp. 33-53, De Frede Editore, Naples, Italy, 1998.

Bogaert, P., M.L. Serre and G. Christakos, "Efficient computational BME analysis of non-Gaussian data in terms of transformation functions". *5th Annual Conference*, Trodheim, Norway, Vol. 1, pp. 57-62, 1999.

Christakos, G., D.T. Hristopoulos, and M.L. Serre, "BME studies of stochastic differential equations representing physical laws-Part I". *5th Annual Conference*, Trodheim, Norway, Vol. 1, pp. 63-68, 1999.

Serre, M.L. and G. Christakos, "BME studies of stochastic differential equations representing physical laws-Part II". *5th Annual Conference*, Trodheim, Norway, Vol. 1, pp. 93-98, 1999.

Application of Statistics & Probability in Soil & Structural Engineering:

Christakos, G., "Stochastic approach and expert systems in the quantitative analysis of soils". *5th International Conference*, Vol. 2, pp. 741-748, Vancouver, Canada, 1987.

EDUCATION

- *Harvard University*, Cambridge, MA, USA: Ph.D. in Applied Sciences (Topic: Generalized random field theory and its application in composite space-time systems modelling and prediction), 1990.
- *National Technical University of Athens*, Athens, Greece: D.Sc. in Mining & Metallurgical Engineering (Topic: GIS-based Geostatistics), 1986.
- *Massachusetts Institute of Technology*, Cambridge, MA, USA: M.S. in Civil & Environmental Engineering (Topic: Kalman filtering in pattern detection and analysis), 1982.
- *University of Birmingham, Birmingham*, UK: M.Sc. in Soil Engineering (Topic: Modelling and experimental investigation of soil-structure interaction during earthquakes), 1980.
- *National Technical University of Athens*, Greece: Diplom (Honors) in Civil Engineering, 1979.

Principal Investigator/Program Director (Last, First, Middle):

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Dr. Daniel Krewski	Professor and Director
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Ottawa, Ottawa, Ontario, Canada	M.H.A.	1988	Health Administration
Carleton University, Ottawa, Ontario, Canada	Ph.D.	1977	Statistics
Carleton University, Ottawa, Ontario, Canada	M.Sc.	1972	Statistics
Carleton University, Ottawa, Ontario, Canada	B.Sc.	1971	Mathematics

NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.

A. **Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

Positions and Employment

1972-74 Statistical Consultant, Survey Design & Statistical Quality Control Section, Food Directorate, Health & Welfare Canada
1974-75 Head, Chemical Statistics Section, Food Directorate, Health & Welfare Canada
1975-76 Student, Carleton University (on educational leave from Health & Welfare Canada
1976-82 Head, Chemical Statistics Section, Food Directorate, Health & Welfare Canada
1987-93 Senior Branch Advisor, Health Risk Assessment, Health Protection Branch, Health & Welfare Canada
1984- Adjunct Research Professor of Statistics, Department of Mathematics and Statistics, Carleton University
1982-94 Chief, Biostatistics and Computer Applications Division, Environmental Health Directorate, Health & Welfare Canada
1995-97 Acting Director, Bureau of Chemical Hazards, Environmental Health Directorate, Health Canada
1997-98 Director, Risk Management, Health Protection Branch, Health Canada
1997- Professor, Department of Medicine and Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa.
2000- Director, McLaughlin Centre for Population Health Risk Assessment, Institute of Population Health, University of Ottawa
2000- Director, Network for Environmental Risk Assessment and Management (Ottawa node)
2002- NSERC/SSHRC/McLaughlin Chair in Population Health Risk Assessment in the Institute of Population Health, University of Ottawa.
2004- Director, Graduate Certificate in Population Health Risk Assessment and Management, Institute of Population Health, University of Ottawa
2005- Director, PAHO-WHO Collaborating Centre for Population Health Risk Assessment, University of Ottawa

Honours:
Elected Fellow of the American Statistical Association (1990); Elected Fellow of the Society for Risk Analysis (1993); Appointed Honorary Senior Research Associate, Division of Epidemiology and Biostatistics, European Institute of Oncology (1994); Elected Vice-Chairman, Scientific Council, International Agency for Research on Cancer (1996); Appointed to Royal Society of Canada Committee on Expert Panels (1996); Canadian Journal of Statistics award for best research paper of the year (1996); Government of Canada Award of Merit (for contributions to renewal of the Canadian Environmental Protection Act); U.S. Environmental Protection Agency Acute Exposure Guideline Levels Team Team Recognition Award (2001) (based on Hammer Award given by Vice-President Gore to EPA to recognize the AEGLs Program); Elected National Affiliate of the U.S. National Academy of Sciences (2002).

Principal Investigator/Program Director (Last, First, Middle): PI Name

Federal Government Committees: Member, U.S. National Academy of Sciences Board on Environmental Studies and Toxicology (1996-2002);Chair, U.S. National Academy of Sciences Committee on Acute Exposure Guidelines for Hazardous Substances (1998-2004); Member, U.S. National Academy of Sciences Committee on Research Priorities for Airborne Particulate Matter (1998-2004). Member, U.S. National Academy of Sciences Committee on Health Effects of Radon (BEIR VI) (1994-1999); Member, U.S. National Academy of Sciences Committee on the Biological Effects of Ionizing Radiation (BEIR VII) (1999-present); Member, U.S. National Academy of Sciences Board on Radiation Effects Research (2000-2005); Chair, U.S. National Academy of Science Committee on Toxicity Testing and Assessment of Environmental agents (2004-present).

B. **Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

Selected Publications 2000-2005 (of 135 publications) and Selected Prior Publications (of 370 publications)

1. Fung,K.Y., Khan,S., Krewski,D., & Ramsay,T. (2006) A comparison of methods for the analysis of recurrent health outcome data with environmental covariates. *Statistics in Medicine*. In press.

2. Chen,Y., Yang,Q., Krewski,D., Burnett,R.T., Shi,Y., & McGrail,K.M. (2005) Difference in effect of course ambient particulate matter on first, second and overall admission for respiratory disease among the elderly. *Inhalation Toxicology*, **17**, 649-655.

3. Fung,K., Krewski,D., Burnett,R., & Dominici,F. (2005) Testing the harvesting hypothesis by time domain regression analysis I: Baseline analysis. *Journal of Toxicology and Environmental Health*, **68**, 1137-1154.

4. Jerrett,M., Burnett,R.T., Ma,R., Thurston,G.D., Newbold,B., Shi,Y., Krewski,D., Finkelstein,N., Pope,A., & Thun,M. (2005) Spatial associations between air pollution and mortality inLos Angeles. *Epidemiology*.

5. Krewski,D., Burnett,R., Goldberg,M.S., Hoover,B.K., Siemiatycki,J., Abrahamowicz,M., Villeneuve,P.J., & White,W.H. (2005) Reanalysis of the Harvard six cities study, Part II: Sensitivity analysis. *Inhalation Toxicology*, **17**, 343-353.

6. Krewski,D., Burnett,R., Goldberg,M.S., Hoover,B.K., Siemiatycki,J., Abrahamowicz,M., & White,W.H. (2005) Reanalysis of the Harvard six cities study, Part I: Validation and replication. *Inhalation Toxicology*, **17**, 335-342.

7. Krewski,D., Burnett,R., Jerrett,M., Pope,C.A., Rainham,D., Calle,E., Thurston,G., & Thun,M. (2005) Mortality and long-term exposure to ambient air pollution: ongoing analyses based on the American Cancer Society cohort. *Journal of Toxicology and Environmental Health*, **68**, 1093-1109.

8. Krewski,D., Dewanji,A., Wang,Y., Bartlett,S., Zielinski,J.M., & Mallick,R. (2005) The effect of record linkage errors on risk estimates in cohort mortality studies. *Survey Methodology*, **31**, 13-21.

9. Liu,S., Krewski,D., Shi,Y., Chen,Y., & Burnett,R. (2005) Association between maternal exposure to ambient air pollutants during pregnancy and fetal growth restriction. *Environmental Health Perspectives*.

10. Yang,Q., Chen,Y., Krewski,D., Burnett,R.T., Shi,Y., & McGrail,K.M. (2005) Effect of short-term exposure to low levels of gaseous pollution on chronic obstructive pulmonary disease hospitalizations. *Environmental Research*, **99**, 99-105.

11. Abrahamowicz,M., du Berger,R., Krewski,D., Burnett,R., Bartlett,G., Tamblyn,R.M., & Leffondre,K. (2004) Bias due to aggregation of individual covariates in the Cox regression model. *American Journal of Epidemiology*, **160**, 696-706.

12. Chen,Y., Yang,Q., Krewski,D., Shi,Y., Burnett,R.T., & McGrail,K. (2004) Influence of relatively low level of particulate air pollution on hospitalization for COPD in elderly people. *Inhalation Toxicology*, **16**, 21-25.

13. Krewski,D., Bakshi,K., Garrett,R., Falke,E., Rusch,G., & Gaylor,D. (2004) Development of acute exposure guideline levels (AEGLs) for airborne exposures to hazardous substances. *Regulatory Toxicology and Pharmacology*, **39**, 184-201.

14. Krewski,D., Burnett,R.T., Goldberg,M.S., Hoover,B.K., Siemiatycki,J., Abrahamowicz,M., & White,W.H. (2004) Validation of the Havard six cities study of air pollution and mortality. *New England Journal of Medicine*, **350**, 198-199.

15. Pope,C.A., Burnett,R.T., Thurston,G.D., Thun,M.J., Calle,E.E., Krewski,D., & Godleski,J.J. (2004) Cardiovascular mortality and long-term exposure to particulate air pollution: Epidemiological evidence of general pathophysiological pathways of disease. *Circulation*, **109**, 71-77.

16. Abrahamowicz,M., Schopflocher,T., Leffondre,K., du Berger,R., & Krewski,D. (2003) Flexible modeling of the exposure-response relationship between long-term average levels of particulate air pollution and mortality in the American Cancer Society study. *Journal of Toxicology and Environmental Health*, **66**, 1625-1654.

17. Burnett,R.T., Dewanji,A., Dominici,F., Goldberg,M.S., Cohen,A.C., & Krewski,D. (2003) On the relationship between time series studies, dynamic population studies, and estimating loss of life due to short-term exposure to environmental risks. *Environmental Health Perspectives*, **111**, 1170-1174.

18. Cakmak,S., Burnett,R., Jerrett,M., Goldberg,M.S., Pope,A., Ma,R., Gultekin,T., Thun,M.J., & Krewski,D. (2003) Spatial regression models for large-cohort studies linking community air pollution and health. *Journal of Toxicology and Environmental Health*, **66**, 1811-1824.

19. Fung,K.Y., Krewski,D., Chen,Y., Burnett,R., & Cakmak,S. (2003) Comparison of time series and case-crossover analyses of air pollution and hospital admission data. *International Journal of Epidemiology*, **32**, 1064-1070.

20. Jerrett,M., Burnett,R.T., Willis,A., Krewski,D., Goldberg,M.S., DeLuca,P., & Finkelstein,N. (2003) Spatial analysis of the air pollution-mortality relationship in the context of ecologic confounders. *Journal of Toxicology and Environmental Health*, **66**, 1735-1778.

21. Krewski,D., Burnett,R., Goldberg,M.S., Hoover,K., Siemiatycki,J., Jerrett,M., Abrahamowicz,M., & White,W.H. (2003) Overview of the re-analysis of the Harvard six cities study and American Cancer Society study of particulate air pollution and mortality. *Journal of Toxicology and Environmental Health*, **66**, 1507-1552.

22. Liu,S., Krewski,D., Shi,Y., Chen,Y., & Burnett,R.T. (2003) Association between gaseous ambient air pollutants and adverse pregancy outcomes in Vancouver, Canada. *Environmental Health Perspectives*, **111**, 1773-1778.

23. Ma,R., Krewski,D., & Burnett,R.T. (2003) Random effects Cox models: A Poisson modelling approach. *Biometrika*, **90**, 157-169.

24. Ramsay,T., Burnett,R.T., & Krewski,D. (2003) The effect of concurvity in generalized additive models linking mortality to ambient particulate matter (with discussion). *Epidemiology*, **14**, 18-23.

25. Ramsay,T., Burnett,R.T., & Krewski,D. (2003) Exploring bias in a generalized additive model for spatial air pollution data. *Environmental Health Perspectives*, **111**, 1283-1288.

26. Siemiatycki,J., Krewski,D., Shi,Y., Goldberg,M.S., Nadon,L., & Lakhani,R. (2003) Controlling for potential confounding by occupational exposures. *Journal of Toxicology and Environmental Health*, **66**, 1591-1604.

27. Villeneuve,P.J., Burnett,R.T., Shi,Y., Krewski,D., Goldberg,M.S., Hertzman,C., Chen,Y., & Brook,J. (2003) A time series study of air pollution, socioeconomic status, and mortality in Vancouver, Canada. *Journal of Exposure Analysis and Environmental Epidemiology*, **13**, 427-435.

28. Willis,A.J., Jerrett,M., Burnett,R.T., & Krewski,D. (2003) The association between sulfate air pollution and mortality at the county scale: An exploration of the impact of scale on a long-term exposure study. *Journal of Toxicology and Environmental Health*, **66**, 1605-1624.

29. Yang,Q., Chen,Y., Shi,Y., Burnett,R.T., McGrail,K., & Krewski,D. (2003) Association between ozone and respiratory admissions among children and the elderly in Vancouver, Canada. *Inhalation Toxicology*, **15**, 1297-1308.

30. Lin,M., Chen,Y., Burnett,R.T., Villeneuve,P., & Krewski,D. (2002) The influence of ambient coarse particulate matter on asthma hospitalization in children: case-crossover and time series analyses. *Environmental Health Perspectives*, **110**, 575-581.

31. Mallick,R., Fung,K., & Krewski,D. (2002) Adjusting for measurement error in the Cox proportional hazards regression model. *Journal of Cancer Epidemiology and Prevention*, **7**, 155-164.

32. Pope,A., Burnett,R.T., Thun,M.J., Calle,E.E., Krewski,D., Ito,K., & Thurston,G.D. (2002) Lung cancer, cardiopulmonary mortality and long-term exposure to fine particulate air pollution. *Journal of the American Medical Association*, **287**, 1132-1141.

33. Villeneuve,P.J., Goldberg,M.S., Krewski,D., Burnett,R.T., & Chen,Y. (2002) Fine particulate air pollution and all-cause mortality within the Harvard Six-cities Study: Variations in risk by period of exposure. *Annals of Epidemiology*, **12**, 568-576.

34. Burnett,R.T., Smith-Doiron,M., Stieb,D., Raizenne,M.E., Brook,J.E., Dales,R.E., Leech.J.A., Cakmak,S., & Krewski,D. (2001) Association between ozone and hospitalization for acute respiratory diseases in children less than 2 years of age. *American Journal of Epidemiology*, **153**, 444-452.

35. Burnett,R.T., Ma,R., Jerrett,M., Goldberg,M.S., Cakmak,S., Pope,A., & Krewski,D. (2001) The spatial association between community air pollution and mortality: A new method of analyzing correlated geographic cohort data. *Environmental Health Perspectives*, **109**, 375-380.

36. Greenbaum,D.S., Bachmann,J.D., Krewski,D., Samet,J.M., White,R., & Wyzga,R.E. (2001) Particulate air pollution standards and morbidity and mortality: Case study. *American Journal of Epidemiology*, **154**, 78S-90S.

C. **Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

1. *Occupational Radiation Carcinogenesis* (**Canadian Institutes of Health Research, 2001-2003, Principal Investigator**). Purpose: To characterize the health risks of occupational exposure to ionizing radiation based on the National Dose Registry of Canada.

2. *Cellular Telephones and Brain Cancer Risk* (**Canadian Institutes of Health Research, 2001-2005, University-industry partnership grant, Principal Investigator**): Purpose: To support Canada's participation in a WHO study of cellular telephones and brain cancer and conduct research on the potential health effects of radiofrequency fields. An international group of scientists assembled by the International Agency for Research on Cancer (IARC) in 1998, recommended that it was justified, feasible and timely to undertake an internationally coordinated study of cancer risks related to cell phone usage. The IARC has undertaken to coordinate such a study and has invited 13 countries to participate. Three Canadian centres have been invited to participate: Montreal, Ottawa and Vancouver/Victoria. These centres were selected by IARC due to a high prevalence of cell phone use, a sufficient number of population-based cases that identified and the availability of a non-biased control group.

3. *Stochastic Models for Radiation Carcinogenesis: Temporal Factors and Dose-Rate Effects* (**U.S. National Institute of Occupational Health and Safety, 2003-2006, Co-investigator, Principal Investigator: Dr. Suresh Moolgavkar**). Purpose: Building on previous work involving the two stage clonal expansion model of carcinogenesis, new stochastic models for radiation carcinogenesis will be developed from two large cohorts: the atomic bomb survivors (100,000 subjects) and the National Dose Registry of Canada (500,000 subjects). Whereas the atomic bomb survivors data involve short term high level exposure to both ionizing radiation, the National Dose Registry involves long term low level exposure. The biologically based models are anticipated to permit an integrated description of the temporal patterns of risk for this two widely divergent exposure scenarios.

4. *Centre for Population Health Risk Assessment* (**R. Samuel McLaughlin Foundation, 2001-2010, Principal Investigator**). Purpose: To develop a new program of research and training in population health risk assessment within the Institute of Population Health. The goal of the Centre is to become a national centre of excellence in population health risk studies, through the development of a unique academic program of research and training in risk studies. This is a field that is underdeveloped in Canada, and the University of Ottawa is well-positioned to assume a leadership role in this area. The Centre will serve as a resource of stakeholders, including government, industry, and the public. The Centre will identify potential risks within a population health context, including

environmental and social & behaviourial risks to the health of Canadian. Risks and attendant uncertainties will be characterized as fully as possible, using the best available methodologies in health risk science. Working with its partners in the federal government, the Centre will articulate and analyze policy option for controlling health risks, thereby contributing to the management of critical population health risks in Canada.

5. *Chair in Population Health Risk Assessment* **(Natural Sciences and Engineering Research Council of Canada/Social Sciences and Humanities Research Council of Canada, 2002-2007, Principal Investigator).** Purpose: To conduct a broad based program of research in population health risks associated with technological change. The NSERC/SSHRC/McLaughlin Chair in Population Health Risk Assessment will further promote the development of risk science, a field that is underdeveloped in Canada. Unique in Canada, the Chair would undertake a comprehensive program of research designed to develop methodologies for the assessment of risks associated with technological development; conduct systematic assessments of the risks associated with specific technologies such as wireless telecommunications and commercial chemicals used by Canadian industry; develop principles to guide risk management decision making and the development of policy options for technological risks; and develop risk communication strategies for technologies for which a comprehensive evaluation of risk has been completed.

6. *Re-analysis of the American Cancer Society Study of Particulate Air Pollution and Mortality, Phase III.* **(Health Effects Institute, 2002-2005, Principal Investigator). Purpose:** To conduct additional analyses of the relationship between urban air pollution and mortality based on the American Cancer Society cohort, with the follow-up period extended from 1982-1989 to 1982-2000 (an additional 11 years of follow-up of this cohort of 1.3 million people). Specific objectives include (1) the development of a multi-level random effects Cox model to describe correlation among the observations, (2) the identification of critical exposure time windows based on a subcohort of 196,000 individuals for which detailed information on population mobility is available, and (3) further analyses of the cohort based on the extended follow-up period.

7. *Air Pollution and Health: A Combined European and North American Approach* **(APHENA / John Hopkins University, School of Public Health, 2003-2005, Co-investigator, Principal Investigator: Dr. Jon Samet).** Purpose: To conduct a combined analysis of North American and European time series studies of particulate air pollution and mortality.

8. *Public Perception and Risk Acceptability* **(Health Canada, 2002-2004, Principal Investigator).** Purpose: To conduct a national survey of health risk perception; to develop a framework for incorporating risk perception into risk management decision making; and to develop guidelines for determining acceptable levels of population health risks.

9. *Health policy approaches to children's environmental health.* **(Health Canada, Principal Investigator).** Purpose: To review the legislative basis for children's environmental health risk management, with particular reference to the Canadian Environmental Protection Act, and the proposed Health Protection Act.

10. *Enhancing Competency Based Performance: A Gender Model for Assessing and Strengthening Health Care Workers' Knowledge, Skills and Resiliency as First Responder* **(CRTI, Co-Investigator, Principal Investigator: Carol Amaratunga).** This project will mitigate the impact of CBRN contagion threats by using lessons learned from SARS to enhance the work performance of front-line health care workers as first responders, through the generation of new knowledge, curriculum development, training, information management and dissemination.

11. *The Role of a General Safety Requirement in Canada's Health Protection Regime.* **(Health Canada Contribution Agreement, 2005-2007, Co-investigator, Principal Investigator: James Benidickson).** Purpose: To utilize international evidence and information on policy options to develop recommendations for the revision and implementation of the Canadian Environmental Protection Act, 1999 and the proposed Canada Health Protection Act.

12. *Occupational and selected non-occupational risk factors for lung cancer: Analysis of a case-control study in Montréal* **(CIHR, 2005-2010, Co-investigator, Principal Investigator: Dr. Jack Siemiatycki).** Purpose: Lung cancer is the most common malignant neoplasm in Canada. A total of 2750 subjects were interviewed, including lung cancer cases and controls. The purpose is to fund a comprehensive program of statistical analysis of the study by conducting multiple parallel sets of analyses that will elucidate the relationship between lung cancer and other classes of variables, such as hundreds of occupational chemicals, alcohol consumption and other variables.

Principal Investigator ____________________

HEI BIOGRAPHICAL SKETCH

Give the following information for professional personnel and consultants beginning with the Principal Investigator. Please do not exceed 2 pages per individual.

NAME	TITLE	BIRTH DATE (*Month, Day, Year*)
Yuanli Shi	Research Associate	Jan. 01, 1961

Education (*Begin with baccalaureate training and include postdoctoral training*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Shanghai Medical University, P.R.China	MD	1979-1984	Public Health
University of Reading, UK	Training	1987-1988	Medical Statistics
University of Reading, UK	MSc	1993-1994	Biometry
University of Salford, UK	PhD Training	1994-1997	Applied Statistics

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: *Concluding with present position, list in chronological order previous employment, experience, and honors. List, in chronological order, the titles and complete references to recent representative publications, especially those most pertinent to this application.*

Positions and Employments:
- Research Associate,
  - McLaughlin Centre for Population Health Risk Assessment,
  - Institute of Population Health,
  - University of Ottawa, Oct.1998 up to now
- Biostatistician,
  - Institute for Cancer Epidemiology,
  - Danish Cancer Society in 1997-98
- Research Associate (1989-93), Research Assistant (1984-89)
  - Division of Epidemiology and Biostatistics, at SIPPR (Shanghai Institute of Planned Parenthood Research) in 1984-93

Professional experience:

Interested in environmental, cancer and reproductive health epidemiology. Working extensively with large population-based survey databases including the American Cancer Society Cancer Prevention Survey II, the National Population Health Survey, the British Columbia Linked Health Datasets, the National or Regional Cancer Registry (Canadian, British and Danish) Data, the Chinese Two-per-thousand Fertility Survey, and the Canadian Enhanced Surveillance for newly identified Hepatitis B and Hepatitis C Virus Infections.

BIOGRAPHICAL SKETCH *continued* Yuanli Shi

List of Publications:

1) Association between maternal exposure to ambient air pollutants during pregnancy and fetal growth restriction. Journal Of Exposure Science And Environmental Epidemiology. (in press)
2) Influence of relatively low level of particulate air pollution on hospitalization for COPD in elderly people. Inhalation Toxicology, 16:1-5, 2004
3) Association between Gaseous Ambient Air Pollutants and Adverse Pregnancy Outcomes in Vancouver, Canada. Environmental Health Perspectives, 2003; Vol. 111 (14): 1773-1778
4) Association between ozone and respiratory admissions among children and the elderly in Vancouver, Canada. Inhalation Toxicology, 2003; 15:101-112
5) A time-series study of air pollution, socioeconomic status and mortality in Vancouver, Canada. Journal of Exposure Analysis and Environmental Epidemiology, 2003,Nov .13(6):427 -35
6) Controlling for potential confounding by occupational exposures. Network for Environmental Risk Assessment and Management (NERAM), Journal of Toxicology and Environmental Health, Oct. 2003;Vol 66 (16-19):1591-1603
7) The Epidemiology of Hepatitis B and Hepatitis C Infection in Canada:1999-2001, IEA World Congress of Epidemiology, Montreal 18-22, August 2002
8) Lung Cancer, Cardiopulmonary Mortality and Long- Term Exposure to Fine Particulate Air Pollution. JAMA. March 6, 2002; 287:1132-1141
9) Incidence of second primary breast cancer among women with a first primary in Manitoba, Canada. Breast Cancer Research and Treatment, 2001; 67: 35-40
10) Krewski, D., Burnett, R. T., Goldberg, M. S., Hoover, K., Siemiatycki, J., Jerrett, M., Abrahamowicz, M., White W. H., et al. 2000. Reanalysis of the Harvard Six Cities study and the American Cancer Society study of particulate air pollution and mortality. Special Report. Cambridge MA: Health Effects
11) Investigator's Report -Part I: Replication and Validation; Part II: Sensitivity Analyses, HEI Publishes Reanalysis of Harvard Six Cities and ACS Studies at HEI web. (http://www.healtheffects.org/news.htm) July 2000
12) Analysis of the time to the first pregnancy after marriage in Shanghai, International Symposium in Shanghai, Oct. 1994
13) Primary cesarean section and its social determinants in Shanghai Municipality, 1994
14) A double blind randomized comparison of two single .doses of mifepristone plus gemeprost for termination pregnancy with amenorrhea between 57 and 63 days, Reproduction and Contraception, Vol. 14(2), 1994 I 15) Breast-feeding and menstrual reversion status for minority women in China, International seminar in Chengdu ofi China, 1993 ! 16) The transition of newly married couples' fertility intention and determinants, Population Research, 1993(1)
17) Suspense and failure in contraception of newly-married couple in Shanghai and the analysis of influential factors, Population Science of China, 1992(6)
18) Premarital sexual activity, pregnancy and contraceptive use status and their influencing factors in Shanghai, Collections of sex education, 1992(10)
19) Analysis of newlyweds' fertility plan and its' shift in Shanghai Municipality, Reproduction and Contraception, Vol. 12(5):38-44, 1992
20) Contraceptive knowledge status and determinants for newly married couples in Shanghai Municipality, Reproduction and Contraception, Vol.12(5):28-37, 1992
21) On the determinants of contraceptive method using by newly married couples, Population Science of China, 1991(5)
22) Factor Analysis of China's Infant Mortality and Its Impact. Population & Economics, 1991 (4)
23) China: fertility intentions strongly affect reproductive behaviour, Progress in Human Reproduction Research, WHO. No.19 1991

EDWARD HUGHES
Consulting in Applied Mathematics and Statistics
Applications Software Development

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Ottawa, Ontario K1R 6H4

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Edward Hughes

Current
Principal of Edward Hughes Consulting.

Education
B.A. (Mathematics) 1965, Rice University, Houston, Texas.
Ph.D. (Mathematics) 1970, University of Wisconsin, Madison.
NRC Postdoctoral Fellowship 1970-71, University of British Columbia, Vancouver.

Areas of Expertise
Consulting in statistics and applied mathematics.
Development of computational software.
Mathematical modelling and simulation in health research, engineering, and economics.
Optimization.

Experience
Design and analysis of a cost-of-production survey for the Canadian Egg Marketing Agency.
Use of survival analysis with time-dependent covariates, on provincial welfare data, to evaluate the effect of a federal-provincial program aimed at reducing welfare spell durations; for the Government of Manitoba and Human Resources Development Canada.
Development of numerical methods and software for a new method of fitting random-effects Cox survival models in epidemiology and reliability studies, for the University of Ottawa Institute of Population Health.
Development of numerical methods and statistical estimation software (random-effects binomial models) for a study of the effects of traffic-related air pollution on cancer incidence, for the McGill University Department of Medicine.
Statistical analysis using the IMDB database to evaluate the "points" system for screening potential immigrants, for Citizenship and Immigration Canada.
Evaluation of survey sampling designs, for Social Development Canada.
Development of an estimation method in pricing of financial derivatives, for a major Canadian financial-services firm.
Statistical analysis using the IMDB database to study immigrant business activity, for Citizenship and Immigration Canada.
Development of methods for optimal stratum allocation in statistical survey sampling design.
Analysis of a cost-allocation model for the Government of British Columbia
Statistical consultant to a major federal study of small-business policy: mainly survey design and analysis.
Development of sampling schemes for inventory management in a large warehouse; this work resulted in a new extension to the method of Dollar-Unit Sampling.
Use of statistical matching methods to evaluate the effect of a government-industry program, for the National Research Council.
Development of methods for statistical sampling and analysis of time series data on landings at airports, to assess the risk-reduction value of various safety regulations.
Development of models for optimal R&D taxation incentives.
Development of new Dollar-Unit Sample evaluation methods for the Auditor-General of Canada.
Development of software for rapid solution of large systems of sparse linear equations.
Estimation of bias in fitting of reliability models arising from human intervention in reporting of failures.
Development of software for reliability and fault-tree analysis.
Development of numerical methods for finite-element modelling.
Numerous projects in finite-element modelling.
Evaluation of numerical methods for field ballistic computations.
Development of a new spectral estimation and smoothing method (and associated software) for a special type of radar data acquisition, which corrects for an error-magnifying distortion in the acquisition process.

Previous Positions

Edward Hughes Consulting started August 1988.
Research Scientist, Ontario Research Foundation, 1984-1988.
Senior Statistical Advisor, Informetrica Ltd., Ottawa, 1980-82 and 1983-84.
Mathematician, Department of Operations Research, Ontario Hydro, 1982-83.
Assistant Professor of Mathematics, Carleton University, Ottawa, 1971-1980.

Professional Activities

More than twenty-five talks, seminars, and refereed articles in various areas of statistics, applied mathematics, and computation.
Statistical Society of Ottawa: President, 1996-97 and 2006-07.
Member, Statistical Society of Canada, American Statistical Association.
Affiliate Scientist, Institute of Population Health, University of Ottawa, from March 2003.

Selected Publications

D. Roland Thomas, Edward Hughes and Bruno D. Zumbo (1998): "On Variable Importance in Linear Regression"; *Social Indicators Research*; v. 45: 253–275.

Edward Hughes, Renjun Ma, Daniel Krewski, Richard T. Burnett (2000): "Computational Algorithm For A Poisson Modelling Approach To Random Effects Cox Models"; Technical report 342, October 2000, Laboratory for Research in Statistics and Probablity, Carleton University, Ottawa. A later version is submitted for publication.

Richard T. Burnett, Michael Jerrett, Renjun Ma, Edward Hughes, C. Arden Pope III, Daniel Krewski (2006): "On the Use of Spatial Survival Models to Examine the Association between Long-Term Exposure to Ambient Air Pollution and Mortality in the American Cancer Society Cohort"; Special symposium *Particulate Air Pollution and Health*, Air and Waste Management Association Annual Meeting, June 2006.

CURRICULUM VITAE

Zev Ross

ZevRoss Spatial Analysis
303 Fairmount Ave – Ithaca, NY 14850
607-277-0004; zev@zevross.com

Education:

M.S. Natural Resources, Minor Biological Statistics; Cornell University, 2003
Thesis - Mapping Disease: A Geostatistical Analysis of California Breast Cancer Rates

B.A. Environmental Studies, Minor Anthropology; Oberlin College, 1995

Work Experience:

President *(May 03-Present)*
ZevRoss Spatial Analysis; Ithaca, NY

- Developed statistical models to predict nitrogen dioxide levels using traffic and land use patterns in San Diego County for the California Department of Health Services.
- Modeled lung function and respiratory symptoms in Juarez, Mexico as a function of air pollution and land use using mixed models for the Centers for Disease Control.
- Developed scripts in SQL to search more than 100,000 free-text biopsy reports for pathologic keywords and generated statistical models to analyze identified cancer cases from veterinary clinics in New York State for the Sprecher Institute for Comparative Cancer Research.
- Contracted by the University of Southern California, Department of Preventive Medicine to develop models to predict fine particulate matter levels in New York City as part of a reanalysis of an American Cancer Society study of air pollution and mortality.
- Used geostatistics, cluster analysis and geographic information systems (GIS) to identify hotspots of arsenic contamination in Bangladesh for Cornell University.
- Contracted by California's Office of Environmental Health Hazard Assessment to refine estimates of exposure to air pollution in Alameda County, California as part of the East Bay Children's Respiratory Health Study.
- Developed logistic models to predict new housing based on physiographic and socioeconomic factors for the Institute for Resource Information Systems in order to identify development pressures on critical vertebrate habitat in New York's Hudson Valley.
- Produced maps and calculated demographics for the Cornell Institute for Economic and Social Research and the City of Ithaca Board of Education as part of the City of Ithaca elementary school redistricting process.
- Generated maps and developed spatial statistical models to identify causes of farmland loss in urban areas nationwide for the Cornell University Department of Development Sociology.

Graduate Research Assistant *(Jan 01-May 03)*
Department of Natural Resources, Cornell University; Ithaca, NY

- Analyzed spatial patterns in more than 170,000 breast cancer incidences in California using spatial statistics, Monte Carlo simulation and GIS.
- One of a limited number of non-California based researchers to be granted permission to work with California Cancer Registry data.

Summer Research Assistant (May 02-Aug 02)
Environmental Health Investigations Branch, Cal. Dept. of Health Services; Oakland, CA

- Completed exposure assessment project evaluating the potential for predicting nitrogen dioxide levels using land use variables such as traffic density and levels of industrialization.
- Used spatial statistics to identify geographic patterns in incidences of breast and testicular cancer.

Analyst (Mar 99-Sep 00)
Environmental Working Group; San Francisco, CA

- Lead author and researcher of widely-distributed statewide studies on lead poisoning, pesticides and indoor air quality. These studies prompted at least 50 articles and editorials in major California newspapers including the Los Angeles Times and two front page Sacramento Bee stories. These studies were also cited by state legislators in decisions to increase funding for the state lead program and to provide funds for indoor air quality research.
- Collected and analyzed state and federal environmental hazard databases including US EPA's Toxics Release Inventory data and California's multi-million record Pesticide Use Reporting data.

Toxics Policy Advocate (May 98-Mar 99)
California Public Interest Research Group; San Francisco, CA

- Lead author and researcher on two statewide pesticide studies leading to more than 50 newspaper articles and editorials and 30 television stories.
- Wrote draft legislation on environmentally healthy schools (passed by California Senate and Assembly, vetoed by Governor Davis).

Conservation Programs Coordinator (Jul 96-May 98)
River Alliance of Wisconsin; Madison, WI

- Researched, wrote and designed reports on river restoration, acid mine pollution and dam removal.
- Research on alternatives to road salt cited by the New York Times and Chicago Tribune.
- Testified and spoke at legislative and public meetings.

Conservation Fellow (Jul 96-May 98)
American Rivers; Washington, DC

- Wrote and researched reports, legal briefs and press releases on the effects of hydropower and mining on river resources.

Awards and Honors:

- Environmental Systems Research Institute Conservation Award (2004)
- City of Ithaca Natural Areas Commission (Appointment by the Mayor in 2003)
- Doris Duke Conservation Fellowship (2002)

Publications:

Ross Z, Duxbury J, DeGloria S, Paul D. 2006. Potential for arsenic contamination of rice in Bangladesh: spatial analysis and mapping of high risk areas. International Journal of Risk Assessment and Management 6(6): 298-315.

Ross Z, English P, Scalf R, Gunier R, Smorodinsky S, Wall S, Jerrett M. 2006. Nitrogen dioxide prediction in Southern California using land use regression modeling: potential for environmental health analyses. Journal of Exposure Science and Environmental Epidemiology 16: 106-114.

Pfeffer M, Francis J, Ross Z. 2006. Fifty years of farmland change: Urbanization, population growth and the changing farm economy. In WA Kandel & DL Brown (eds.), Population Change and Rural Society: 103-129.

Under Review
Ross Z, Ito K, Tempalski B, Thurston G, Jerrett M. 2006. A land use regression for predicting fine particulate matter concentrations in the New York City region. Atmospheric Environment.

In Prep for 2007
Waller L, Wang Y, Ross Z. Spatial analysis of Anasazi sites in Black Mesa, Arizona.

Waller L, Ross Z. Quantifying the impact of uncertain locations in tests of focused clustering: another look at leukemia and TCE sites in upstate NY.

Somberg L, Smorodinsky S, Scalf R, Gunier R, English P, Ross Z. 2006. Assessment of exposure to traffic pollution: effects misclassification by six methods.

Reports and Briefs:

Ross, Z. 2004. *Understanding Breast Cancer Rates.* Cornell University College of Veterinary Medicine, Program on Breast Cancer and Environmental Risk Factors; Ithaca, NY.

Ross, Z. 2003. *Mapping Disease: Deciphering Geographic Patterns From Cholera to Breast Cancer.* Cornell University College of Veterinary Medicine, Program on Breast Cancer and Environmental Risk Factors; Ithaca, NY.

Ross, Z, Walker, B and Wiles, R. 2000. *Lead Astray: California's Broken Promise to Protect Kids from Lead Poisoning.* Environmental Working Group; Washington, DC.

Ross, Z and Walker, B. 2000. *Uncontrolled LUSTs: Leaking Fuel Storage Tanks Threaten Water, But State Lets Oil Companies Off the Hook.* Environmental Working Group; Washington, DC.

Ross, Z and Walker, B. 2000. *An Ill Wind: Methyl Bromide Use Near California Schools.* Environmental Working Group; Washington, DC.

Ross, Z and Walker, B. 1999. *Reading, Writing and Risk: Air Pollution Inside California's Portable Classrooms.* Environmental Working Group; Washington, DC.

Ross, Z. 1999. *Toxic Fraud: Deceptive Advertising by Pest Control Companies.* California Public Interest Research Group and Californians for Pesticide Reform; San Francisco, CA.

Ross, Z and Kaplan, J. 1998. *Poisoning the Air: Airborne Pesticides in California.* California Public Interest Research Group and Californians for Pesticide Reform; San Francisco, CA.

Gray, S, Ross, Z and Walker, B. 2001. *Every Breath You Take: Airborne Pesticides in the San Joaquin Valley.* Environmental Working Group; Washington, DC.

Smith, V, Coequyt, J and Ross, Z. 2000. *Clean Water Report Card: Water quality permitting in Cali gets a failing grade.* Friends of the Earth and Environmental Working Group; Washington, DC.

Coequyt, J, Wiles, R and Ross, Z. 1999. *Above the Law: How California's Major Air Polluters Get Away With It.* Environmental Working Group; Washington, DC.

Kaplan, J, Ross, Z and Walker, B. 1999. *As You Sow: Toxic Waste in California Home and Farm Fertilizers.* California Public Interest Research Group and Environmental Working Group; San Francisco, CA.

Principal Investigator/Program Director (Last, first, middle): ____________

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow this format for each person. DO NOT EXCEED FOUR PAGES.

NAME	POSITION TITLE
George D. Thurston	Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Brown University, Providence, RI	Sc.B.	1974	Environ. Engineering
Brown University, Providence, RI	A.B.	1974	Environ. Studies
Harvard University, Cambridge, MA	M.S.	1978	Environ. Health Sci.
Harvard University, Cambridge, MA	Sc.D.	1983	Environ. Health Sci.

A. Positions and Honors

Positions and Employment

1974-1977 Engineer, Hittman Associates, Inc., Energy and Environmental Systems Department, Columbia, MD
1978-1982 Researcher, Harvard University School of Public Health, Dept. of Environ. Health, Boston, MA
1982-1984 Research Fellow, Harvard University, Kennedy School of Government, Health & Environmental Policy Center, Cambridge, MA
1984-1987 Research Assistant Professor, Department of Environmental Medicine, New York University School of Medicine, New York, NY
1987-1993 Assistant Professor, Department of Environmental Medicine, New York University School of Medicine, New York, NY
1993-pres Associate Professor (Tenured), Department of Environmental Medicine, New York University School of Medicine, New York, NY
1995-pres Director, Community Outreach and Education Program, NIEHS Center of Excellence, New York University School of Medicine, New York, NY
2002-pres Deputy Director, NYU-EPA Particulate Matter Center, NYU School of Medicine, New York, NY

Other Experience and Professional Memberships

American Thoracic Society (Environ. and Occup. Health Program Committee)
International Society for Environmental Epidemiology
International Society of Exposure Analysis (Associate Editor: J. Exp. Anal. Environ. Epidemiol. (1993-present)
National Academy of Sciences, Committee on Health Effects of Waste Incineration (1/95-1/2000)
ATS/ALA National Air Conservation Commission Member (1997-2000); Chairman, Health and Environmental Impact Assessment Panel, Joint Canadian Industry/Government Study of Sulphur in Gasoline and Diesel Fuels (9/96-6/97)

B. Selected peer-reviewed publications

Thurston, G.D. and Laird, N. Letters: Tracing aerosol pollution. Science 227:1406-1408 (1985).
Thurston, G.D. and Spengler, J.D. A quantitative assessment of source contributions to inhalable particulate matter in metropolitan Boston, MA. Atmos. Environ. 19:9-25 (1985).
Ozkaynak, H. and Thurston, G.D. Associations between 1980 U.S. mortality rates and alternative measures of airborne particle concentration. Risk Anal. 7:449-460 (1987).
Spektor, D.M., Lippmann, M., Lioy, P.J., Thurston, G.D., Citak, K., James, D.J., Bock, N., Speizer, F.E., and Hayes, C. Effects of ambient ozone on respiratory function in active normal children. Am. Rev. Respir. Dis. 137:313-320 (1988).
Lippmann, M. and Thurston, G.D. Exposure assessment - Input into risk assessment. Arch. Environ. Health 43:113-123 (1988).
Spektor, D.M., Lippmann, M., Thurston, G.D., Lioy, P.J., Stecko, J., O'Connor, G., Garshick, E., Speizer, F.E., and Hayes, C. Effects of ambient ozone on respiratory function in healthy adult exercising outdoors. Am. Rev. Respir. Dis. 138:821-828 (1988).
Thurston, G.D, Ito, K., Lippmann, M., and Hayes, C. Re-examination of London mortality in relation to exposure to acidic aerosols during 1962-1973 winters. Environ. Health Perspect. 79:73-82 (1989).
Spektor, D.M., Hofmeister, V.A., Artaxo, P., Brague, J., Echelar, F., Nogueira, D.P., Hayes, C., Thurston, G.D., and Lippmann, M. Effects of heavy industrial pollution on respiratory function in the children of Cubatao, Brazil: A preliminary report. Environ. Health Perspect. 94:51-54 (1991).

Spektor, D.M., Thurston, G.D., Mao, J., He, D., Hayes, C., and Lippmann, M.
ozone exposures on respiratory function in active normal children. Environ.

Thurston, G.D. and Ozkaynak, H. Letters: Air pollution and mortality. Science 225:382-383 (19

Thurston, G.D., D'Souza, N., Lippmann, M., Bartoszek, M., and Fine, J. Associations between summer haze air pollution and asthma exacerbations: A pilot camp study. Am. Rev. Respir. Dis. 145:A429 (1992).

Thurston, G.D., Ito, K., Kinney, P., and Lippmann, M. A multi-year study of air pollution and respiratory hospital admissions in three New York State metropolitan areas: Results for 1988 and 1989 summers. J. Expos. Anal. Environ. Epidemiol. 2:429-450 (1992).

Ito, K., Thurston, G.D., Hayes, C., and Lippmann, M. Associations of London, England daily mortality with particulate matter, sulfur dioxide, and acidic aerosol pollution. Arch. Environ. Health 48:213-220 (1993).

Thurston, G.D., Ito, K., Lippmann, M., and Bates, D.V. Respiratory hospital admissions and summertime haze air pollution in Toronto, Ontario: Consideration of the role of acid aerosols. Environ. Res. 65:271-290 (1994).

Kinney, P.L., Ito, K., and Thurston, G.D. A sensitivity analysis of mortality/PM10 associations in Los Angeles. Inhal. Toxicol. 7:59-69 (1995).

Thurston, G.D. and Kinney, P.L. Air pollution epidemiology: Considerations in time-series modeling. Inhal. Toxicol. 7:71-83 (1995).

Ito, K. and Thurston, G. Daily PM10/mortality associations: An investigation of at-risk subpopulations. J. Expos. Anal. Environ. Epidemiol. 6:79-96 (1996).

Thurston, G.D. A critical review of PM10-mortality time-series. J. Expos. Anal. Environ. Epid.. 6:3-22 (1996).

Kinney, P.L., Thurston, G.D., and Raizenne, M. The effects of ambient ozone on lung function in children: A reanalysis of six summer camp studies. Environ. Health Perspect. 104:170-174 (1996).

Thurston, G.D., Lippmann, M., Scott, M.B., and Fine, J.M. Summertime haze air pollution and children with asthma. Am. J. Respir. Crit. Care Med. 155:654-660 (1997).

Cassino, C., Ito, K., Bader, I., Ciotoli, C., Thurston, G., and Reibman, J. Cigarette smoking and ozone-associated emergency department use for asthma by adults in New York City. Am. J. Respir. Crit. Care Med. 159:1773 (1999).

Gwynn, R.C., Burnett, R.T., and Thurston, G.D. A time-series analysis of acidic particulate matter and daily mortality and morbidity in the Buffalo, New York, region. Environ. Health Perspect. 108(2):125-133 (2000).

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BIOGRAPHICAL SKETCH

NAME
Pope, C. Arden III

POSITION TITLE
Professor of Economics, BYU

EDUCATION

Institution	Degree	Year Graduated	Fields of Study
Brigham Young University	B.S.	1978	Ag.Econ/English
Iowa State University	M.S.	1981	Economics
Iowa State University	Ph.D.	1981	Economics/Statistics

A. POSITIONS and HONORS

Positions and Employment

1980-1982	Research Associate/Staff Economist, Department of Economics, Center for Agricultural and Rural Development, Iowa State University.
1982-1984	Assistant Professor, Department of Agricultural Economics, Texas A & M University.
1984-1988	Assistant/Associate Professor, Agricultural Economics Department, Brigham Young University.
1988-1994	Associate Professor, Economics Department, Brigham Young University.
1992-1993	Visiting Scientist, Environmental Epidemiology Program, Department of Environmental Health, Harvard School of Public Health, Harvard University.
1994-present	Full Professor, Economics Department, Brigham Young University.

Selected Honors

1986	Creative Achievement Award, College of Biology and Agriculture, Brigham Young University.
1992/1993	IPH Fellow, Environmental Health and Public Policy, Harvard University.
1995	Karl G. Maeser, Excellence in Research and Creative Arts Award, Brigham Young University.
1997	Clarence Olds Sappington Memorial Lecturer, American College of Occupational and Environmental Medicine.
2000	*Sigma Xi* Lecturer Award, *Sigma Xi* Scientific Research Society, Brigham Young University Chapter.
2001	Thomas T. Mercer Joint Prize, The American Association for Aerosol Research, and The International Society for Aerosols in Medicine.
2004	Utah Governor's Medal for Science & Technology
2005	Mary Lou Fulton Professorship, Brigham Young University.
2006	Karl G. Maeser Distinguished Faculty Lecturer, Brigham Young University.

B. SELECTED RESEARCH PUBLICATIONS

Pope CA III. Respiratory disease associated with community air pollution and a steel mill. *The American Journal of Public Health* 79(1989):623-628.

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Pope CA III, Kalkstein LS. Synoptic weather modeling and estimates of the exposure-response relationship between daily mortality and particulate air pollution. *Environmental Health Perspectives* 104(1996):414-420.

Pope CA III, Adverse health effects of air pollution in a nonsmoking population. *Toxicology* 111(1996):149-155.

Pope CA III, Schwartz J. Time series for the analysis of pulmonary health data. *American Journal of Respiratory and Critical Care Medicine* 154(1996):S229-S233.

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Hoek G, Dockery DW, Pope CA III, Neas L, Roemer W, Brunekreef B. Association between PM_{10} and decrements in peak expiratory flow rates in children: reanalysis of data from five panel studies. *European Respiratory Journal* 11(1998):1307-1311.

Gold DR, Damokosh AI, Pope CA III, Dockery DW, McDonnell WF, Serrano P, Retama A, Castillejos M. Particulate and ozone pollutant effects on the respiratory function of children in southwest Mexico City. *Epidemiology* 10(1999):8-16.

Pope CA III, Dockery DW, Kanner RE, Villegas GM, Schwartz J. Oxygen saturation, pulse rate, and particulate air pollution: a daily time-series panel study. *American Journal of Respiratory and Critical Care Medicine* 159(1999):365-372.

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