ELECTRIC POWER RESEARCH INSTITUTE

March 26, 2009

Dr. Holly Stallworth
Designated Federal Officer
EPA Science Advisory Board (1400F)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: PM ISA Comments for CASAC Meeting, April 1-2, 2009

Dear Dr. Stallworth:

Attached please find comments on the First External Review Draft of the Integrated Science Assessment for Particulate Matter, prepared by the Electric Power Research Institute (EPRI). I have also attached a paper currently in press (Lipfert et al., 2009) that is referenced in our comments.

Sincerely,

Annette C. Rohr, ScD, DABT
Senior Technical Manager, Air Quality and Health

Attachments

PALO ALTO OFFICE
3420 Hillview Avenue, Palo Alto, CA 94304-1338 USA • 650.855.2000 • Customer Service 800.313.3774 • www.epri.com

COMMENTS ON THE INTEGRATED SCIENCE ASSESSMENT FOR PARTICULATE MATTER FIRST EXTERNAL REVIEW DRAFT

Annette C. Rohr, Sc.D.
(650) 855-2765
arohr@epri.com

Ronald E. Wyzga, Sc.D.
(650) 855-2577
rwyzga@epri.com

Electric Power Research Institute (EPRI)
3420 Hillview Ave
Palo Alto, CA 94304

April 1, 2009

Overall, the ISA is a generally thorough, balanced, and well-written summary of the existing PM health literature. However, we do have some significant concerns as follows:

1. The discussion of the accumulated evidence for specific PM components and health impacts is limited in the ISA compared with previous Criteria Documents for PM, despite the significant recent literature on this issue. **Much more emphasis should be placed on this topic in the ISA.** As PM composition clearly influences resultant toxicity, it would behoove the Agency to evaluate the feasibility of a regulatory paradigm that emphasizes those components that are of most concern from a health perspective. The first step in such an activity is to compile all available information and review it to evaluate weight-of-evidence; the result of such an evaluation should be included in the ISA. This is particularly true given the Agency's application of causality criteria for PM size metrics in the ISA; this application should be extended to PM components.

2. In particular, Section 2.3.3 inaccurately characterizes the literature related to PM composition and health effects. The section is termed "$PM_{2.5}$ Constituents or Sources Linked to Health Outcomes"; however, the table only includes studies that use factor analytical approaches in the context of the complex PM mixture. The numerous epidemiological and toxicological studies that have examined specific components in the absence of such analyses are not mentioned and should be included (e.g., Klemm et al., 2004; Metzger et al., 2004; Peel et al., 2005; Peel et al., 2007; Sinclair and Tolsma, 2004; Tolbert et al., 2000; Ostro et al., 2009; citations provided at end of comments). We also note that the results of Laden et al.. (2000) are incorrectly cited here and elsewhere in the ISA. In the reanalysis (Schwartz, 2003), the association between mortality and the coal combustion source factor was no longer statistically significant.

3. We note that in many cases, human or animal exposures to complex mixtures (e.g., DE, woodsmoke) are included as evidence of PM-related effects. In some cases, filtration was conducted to allow attribution of observed effects to either PM or gas-phase materials; however, in most cases this was not done. It is therefore difficult to characterize PM as the sole causative agent in these studies. Furthermore, and along the lines of our comment 1 above, although many of the studies cited in the ISA used traffic or diesel exhaust as estimates of exposure, no attempt was made to integrate the results for these metrics.

4. The issue of co-pollutants is rarely addressed comprehensively in the ISA, and there is a need to consider all potential co-pollutants systematically. There is also the possibility that measured pollutants may be serving as surrogates for substances that are not routinely measured. For example, a paper in press (Lipfert et al., 2009; attached to these comments) reports that several non-criteria air pollutants appear to be more highly associated with premature mortality than the NAAQS pollutants.

Selected Specific Comments:

Chapter 5

p. 5-13: The involvement of trigeminal nerve-mediated responses (sensory irritation) in the upper airways should be included here as these responses affect both respiratory pattern as well as cardiovascular function. There is a large literature on this well-studied response, including the following:

Alarie, Y. 1973. Sensory irritation by airborne chemicals. *CRC Crit Rev Toxicol* 2:299-363.

Nielsen, G.D. 1991. Mechanisms of activation of the sensory irritant receptor by airborne chemicals. *Crit. Rev. Toxicol.* 21:183-208.

Chapter 6:

Note: Seagrave et al. (2008) should be included in the relevant sections of Chapter 6 (both respiratory and cardiovascular endpoints).

Seagrave, J.C., Campen, M.J., McDonald, J.D., Mauderly, J.L., and Rohr, A.C. 2008. Oxidative stress, inflammation, and pulmonary function assessment in rats exposed to laboratory-generated pollutant mixtures. *J. Toxicol. Environ. Health, Part A* 71:1352-1362.

p. 6-17, 2nd full paragraph: Routledge et al. (2006) exposed human volunteers to ultrafine elemental carbon/carbon black. This should be reflected in the discussion, and the generic term "carbon" modified. Certainly there was no organic carbon involved in the exposures. Moreover, the conclusion of the study, as stated by the authors, was that "The adverse effects of vehicle derived particulates are likely to be caused by more reactive species found on the particle surface", which is rather different from that expressed in lines 27-30 of the ISA.

p. 6-30, 1st full paragraph: The comparison of the work of Anselme et al. (2007) with Wellenius et al. is invalid and inappropriate given that each investigated a different PM source (Anselme DE, Wellenius ROFA).

p. 6-31, lines 18-19: Not sure how this statement is relevant, given that DE-filtered atmospheres (with virtually zero PM) induced effects.

p. 6-37: The Dales et al. and Rundell et al. studies both implicate traffic, and there could be other dimensions of this exposure besides PM that explain the result.

p. 6-40, lines 5-7: There are numerous gas-phase and SV organic compounds as well in DE.

p. 6-61: The Reidiker et al. study examined specific components of PM; this should be noted.

p. 6-65, 1st full paragraph: In addition to the factors stated at the end of the paragraph, PM composition is likely to strongly influence results.

p. 6-69: Again, the section organization is inconsistent. “PM Components” is included as a separate subsection for toxicological studies of oxidative stress, but is not consistently presented for other endpoints (or other study approaches, i.e., epidemiology, clinical studies).

p. 6-76: Metzger et al. (2004) also analyzed PM and its components jointly with CO and NO_2, both of which appeared to be stronger predictors of ED visits. It should be noted that Sarnat et al. (2008) used a different set of lags than did Metzger et al.

p. 6-82, lines 19-20: There is inconsistent presentation of results in the document. Here, the ISA states that positive associations were observed but did not reach statistical significance; however, other studies’ findings are not consistently described in this manner.

p. 6-88, lines 12-17: Metzger et al. (2007) should be included in this section.

p. 6.89, lines 1-4: See above comments for Metzger et al. (2004).

p. 6-126, Section 6.3.2.3: This section needs to consider and discuss trigeminal nerve stimulation, i.e., sensory irritation (see comment above).

p. 6-141, 1st paragraph: The greater toxicologic potency of urban particles in Schaumann et al. (2004) could also be due to a greater contribution of organic material, not only to greater concentration of transition metals.

p. 6-145, 1st paragraph: The ISA should discuss the limitations and caveats of the monocrotaline model and its representiveness to human disease.

p. 6-151: Because collected coal fly ash (e.g., from an electrostatic precipitator) is by its nature material that has been retained and does not enter the atmosphere, its relevance to human exposure is unclear. Moreover, emissions generated from lab-scale combustors differ significantly from full-scale plant emissions due to (a) difference in time-temperature histories; and (b) the lack of pollution control equipment such as ESPs, SCRs, and FGD systems.

p. 6-154, lines 15-18: Besides a greater proportion of UF particles near roadways, there are also elevated concentrations of traffic-related pollutants in general, including gas-phase compounds and other PM size fractions.

p. 6-159, “Summary”: Virtually all the studies presented in the ISA in the section on allergic sensitization were conducted with diesel emissions; therefore, stating that “PM can modulate immune reactivity” may potentially be overstating the effect. Clearly DE can induce this effect; however, the evidence for ambient PM, or, for that matter, diesel PM, eliciting this response is less certain. Diesel emissions contain a plethora of non-PM pollutants.

p. 6-160: Again, for host defense, the bulk of the studies were conducted with DEP.

p. 6-168, ll. 16-26: It should be noted that Peel et al. (2005) and Sarnat et al. (2008) used different lags. A detailed examination of results by lag in Peel at al. shows no conflict with the Sarnat et al. results.

p. 6-174 and follows: Sinclair and Tolsma (2004) also examined physician visits for adult asthmatics and found no significant positive associations.

p. 6-180: Sinclair and Tolsma (2004) also examined physician visits for upper and lower respiratory diseases.

p. 6-182, lines 4-17: Peel et al. (2005) needs to be considered in this regard.

p. 6-229 (Section 6.5.2.5): This section is missing the results of Klemm et al. (2004).

p. 6-236: Those findings that are statistically significant should be noted and distinguished from those that are not. It is also important to indicate that the factor loading are for the "source factors"; the names of these factors can be misleading. Ideally, a comparison of epidemiological analyses using source apportioned data and analyses using single component data will help to evaluate consistency.

p. 6-242 and following: This section needs also to consider other metrics that have been considered in the ISA; e.g., traffic, diesel particles, etc.

p. 6-245, line 16: It should be noted that the Laden et al. (2000) findings changed with the Schwartz (2003) reanalysis.

p. 6-246, lines 7-8: A comparison of the results of this study with those of Peel et al. (2005) demonstrates that the choice of lag was key. Significant results of opposite signs were reported for sulfate by Peel et al.

p. 6-246, line 23: Metzger et al. (2004) also considered PM components.

p. 6-246, lines 27-30: These studies are discussed in Chapter 7 of the ISA, and, as long-term studies, should not be included here.

p. 6-247 and follows: Several studies are missing – e.g., Peel et al (2005); Metzger et al (2004); Sinclair and Tolsma (2004); Klemm et al. (2004).

p. 6-247: Again, the Laden et al. (2000) reference is incorrectly stated. The Schwartz (2003) reanalysis found that the coal source factor was no longer significant.

Chapter 7:

p. 7-38, lines 19-20: Brown Norway rats are only an allergic model if they are sensitized, typically using an ovalbumin protocol; this should be stated.

p. 93, lines 8-9: Again, care should be taken to adequately characterize the risk posed by diesel PM vs. other non-PM materials present in diesel emissions/exhaust.

p. 7-100, Summary: It should be noted that many of the exposures conducted were to mixtures of PM and gas-phase compounds. In particular, the ISA states that studies were conducted of DEP, but in fact most of those studies were of DE.

p. 7-100, line 20: What is meant by "broadly representative"? No cohort is completely representative. The Six Cities Study, for example, looked at only a quadrant of the US, and the ACS cohort was above-average socioeconomically.

p. 7-102, Table 7-8: Additional studies should be added to this table and accompanying discussion:

Enstrom, J.E. 2005. Fine particulate air pollution and total mortality among elderly Californians, 1973-2002. *Inhal Toxicol.* 17:803-16.

Jerrett, M., Newbold. K.B., Burnett, R.T., Thurston, G., Lall, R., Pope, C.A. III, Ma, R., De Luca, P., Thun, M., Calle, J., Krewski, D. 2007. Geographies of uncertainty in the health benefits of air quality improvements; *Stoch Environ Res Risk Assess* . 21:511-522.

Lipfert, F.W., Baty, J.D., Miller, J.P., Wyzga, R.E.. 2006. $PM_{2.5}$ constituents and related air quality variables as predictors of survival in a cohort of U.S. military veterans; *Inhal Toxicol.* 18:645-657 (should be included under $PM_{2.5}$ results).

Lipfert, F.W., Wyzga, R.E., Baty, J.D., Miller, J.P. 2006. Traffic density as a surrogate measure of environmental exposures in studies of air pollution health effects: Long-term mortality in a cohort of US veterans. *Atmos Environ.* 40:154-169 (also presents results for $PM_{2.5}$).

Several of the above also address the issue of components, which could be summarized here as well.

p. 7-103, Figure 7-7: This table should also include Jerrett et al. (2007), provided above.

p. 7-110, line 15-16: This phrasing is not consistent throughout the document. If positive but nonsignificant results are highlighted, this should be done for all pollutants in all studies. This paragraph should take note of the recently accepted paper by Lipfert et al. (attached and referenced in comments for p 7-108.)

p. 7-115: In this discussion of the expert judgment study (Roman et al., 2008), the European expert judgment should also be included (Cooke et al., 2007).

Cooke, R.M., Wilson, A.M., Tuomisto, J.T., Morales, O., Tainio, M., and Evans, J.S. 2007. A probabilistic characterization of the relationship between fine particulate matter and mortality: elicitation of European experts. *Environ. Sci. Technol*. 41:6598-6605.

Chapter 8:

p. 8-15, Section 8.2.1.10: Toxicological studies using the JCR (prediabetic) rat model should be included here, e.g., Proctor et al., 2006.

Proctor, S.D., Dreher, K.L., Kelly, S.E., and Russell, J.C. 2006. Hypersensitivity of prediabetic JCR:LA-cp rats to fine airborne combustion particle-induced direct and nonadrenergic-mediated vascular contraction. *Toxicol. Sci.* 90:385-391.

References Cited

Klemm, R.J., Lipfert, F.W., Wyzga, R.E., and Gust, C. 2004. Daily mortality and air pollution in Atlanta: two years of data from ARIES. *Inhal. Toxicol*. 16(suppl 1):131-141.

Metzger, K., Tolbert, P., Klein, M., Peel, J., Flanders, W., Todd, K., Mulholland, J., Ryan, P., Frumkin, H. 2004. Ambient air pollution and cardiovascular emergency department visits. *Epidemiology* 15(1): 46-56.

Ostro, B., Roth, L., Malig, B., and Marty, M. 2009. The effects of fine particle components on respiratory hospital admissions in children. *Environ. Health Perspect*. 117(3):475-480.

Peel, J. L., Tolbert, P.E., Klein, M., Metzger, K.B., Flanders, W.D., Todd, K., Mulholland, J.A., Ryan, P.B., Frumkin, H. 2005. Ambient air pollution and respiratory emergency department visits. *Epidemiology* 16(2):164-174.

Peel, J., Metzger, K., Klein, M., Flanders, W., Mulholland, J., Tolbert, P. 2007. Ambient air pollution and cardiovascular emergency department visits in potentially sensitive groups. *Am. J. Epidemiol.* 165(6):625-633.

Sinclair, A., Tolsma, D. 2004. Associations and lags between air pollution and acute respiratory visits in an ambulatory, care setting: 25-month results from the Aerosol Research and Inhalation Epidemiology Study. *J. Air Waste Manage. Assoc*. 54(9):1212-1218.

Tolbert, P.E., Klein, M., Metzger, K.B., Peel, J., Flanders, W.D., Todd, K., Mulholland, J.A., Ryan, P.B., Frumkin, H. 2000. Interim results of the Study of Particulates and Health in Atlanta (SOPHIA). *J. Exp. Anal. Environ. Epidemiol.* 10(5):446-460.

Air Pollution and Survival within the Washington University - EPRI Veterans Cohort: Risks Based on Modeled Estimates of Ambient Levels of Hazardous and Criteria Air Pollutants (Accepted by J.AWMA, Nov 12, 2008)

F.W. Lipfert[1], R.E. Wyzga[2], Jack D. Baty[3], J. Phillip Miller[3]

[1]Consultant, Northport, NY
[2]Technical Executive, Electric Power Research Institute, Palo Alto, CA
[3]Division of Biostatistics, School of Medicine, Washington University, St. Louis, MO

ABSTRACT

We considered relationships between mortality, vehicular traffic density, and ambient levels of twelve hazardous air pollutants, elemental carbon, NO_x, SO_2, and SO_4^{2-}. These pollutant species were selected as markers for specific types of emission sources, including vehicular traffic, coal combustion, smelters, and metal-working industries. Pollutant exposures were estimated using emissions inventories and atmospheric dispersion models. We analyzed associations between county ambient levels of these pollutants and survival patterns among ~70,000 US male veterans, by mortality period (1976-2001 and subsets), type of exposure model, and traffic density level. We found significant associations between all-cause mortality and traffic-related air quality indicators and with traffic density per se, with stronger associations for benzene, formaldehyde, diesel particulate, oxides of nitrogen, and elemental carbon. The maximum effect on mortality for all cohort subjects during the 26-y follow-up period is about 10%, but most of the pollution-related deaths in this cohort occurred in the higher-traffic counties, where excess risks approach 20%. However, mortality associations with diesel particulates are similar in high- and low-traffic counties. Sensitivity analyses show risks decreasing slightly over time and minor differences between linear and logarithmic exposure models. Two-pollutant models show stronger risks associated with specific traffic-related pollutants than with traffic density per se, although traffic density retains statistical significance in most cases. We conclude that tailpipe emissions of both gases and particles are among the most significant and robust predictors of mortality in this cohort and that most of those associations have weakened over time. However, we have not evaluated possible contributions from road dust or traffic noise. Stratification by traffic density level suggests the presence of response thresholds, especially for gaseous pollutants. Because of their wider distributions of estimated exposures, risk estimates

based on emissions and atmospheric dispersion models tend to be more precise than those based on local ambient measurements.

IMPLICATIONS

This research confirms the importance of residence in high-traffic counties on long-term survival within this cohort of male military veterans. It shows robust risk estimates based on spatially-averaged gas and particle concentrations estimated from emissions and atmospheric dispersion modeling, rather than from ambient measurements. There are important differences in the risks attributed to these pollutants that indicate the importance of hazardous and non-criteria species in explaining associations between air quality and survival. Mortality risks also differ by mortality follow-up period and level of traffic density. For most pollutants, stronger risk coefficients occur in the high-traffic density counties, suggesting exposure thresholds.

INTRODUCTION

Prospective cohort studies have become the "gold standard" for epidemiological studies of long-term health effects of air pollution. Most of these studies are limited by the availability of the ambient air quality data required to estimate subjects' exposures to the pollutants of interest. Exposure estimates for most cohorts have been based on outdoor ambient conditions where subjects resided at entry to the study. Limitations include the numbers and locations of air monitoring sites, their periods of operation, and the species monitored. For example, the American Cancer Society (ACS) study,[1,2] which played an important role in establishing the National Ambient Air Quality Standard (NAAQS) for $PM_{2.5}$, used $PM_{2.5}$ monitoring data from only 51 locations and assigned each of them to a multi-county metropolitan statistical area. This reduced the population under study by about 75%. Subsequent reanalysis of these results[3] found SO_2 to be a more robust predictor of mortality in this cohort than either $PM_{2.5}$ or SO_4^{2-}, even though SO_2 is known to exhibit strong local concentration gradients and its implied health effects are problematic at these low concentration levels. Analysis of more localized $PM_{2.5}$ levels in Southern California and New York City metropolitan areas, obtained by spatial interpolation of the available measurements, showed much stronger within-city mortality effects,[4,5] suggesting local rather than regional effects.

In previous papers, the Washington University-EPRI Veterans Cohort Mortality Study considered a wide range of measured ambient air quality data at the (single) county level, including various $PM_{2.5}$ constituents from the Speciation Trends Network (STN)[6,7] initiated by the U.S. Environmental Protection Agency (EPA) in 1999. We also considered county-level vehicular traffic density, computed as annual vehicle-distance traveled per unit of county land area; we found this parameter to be the most robust predictor of survival for this cohort.[7-9] However, traffic density may represent a wide range of potentially causal agents, including emissions of combustion products, degradation products from vehicle or roadway wear, traffic noise, stress, and socioeconomic effects associated with preferred residential locations, but it is not specific to any of them. A previous paper[9] considered sensitivity to the mathematical form of the exposure variable (linear, logarithmic, or categorical) and concluded that the results were

not sensitive to the choice of continuous measure (linear vs. logarithmic). However, larger risks are seen in the more urban counties, as characterized by traffic density levels. Also, estimating and accumulating effects over several sub-periods of mortality follow-up yields larger mortality risks than analyzing the entire follow-up period in a single regression.

This paper considers the unresolved question: does the success of traffic density as a predictor of survival in this cohort derive from the availability of data for each county in the contiguous United States? An additional rationale could be that this surrogate exposure metric represents a county average rather than a point estimate and thus is not subject to the vagaries of site selection for ambient air quality monitoring stations. We draw upon two sources of national annual-average county-level ambient air quality data to consider these questions:

1. County-average ambient levels of selected hazardous air pollutants, from EPA's National Air Toxics Assessment (NATA).[10,11] These data are referred to here as "HAPS" values, and we selected 12 of them for detailed analyses of their associations with the veterans' survival, based on their likely associations with different types of emission sources, including vehicular traffic, coal combustion sources, smelters, and metal-working industries.

2. Estimates from the plume-in-grid model of Atmospheric and Environmental Research, Inc.[12-14] for SO_2, NO_x, sulfate aerosol (as $(NH_4)_2SO_4$), and elemental carbon (EC). These data are referred to as "AER" values. These species were selected because they have been found to be important in other cohort studies[1-7] and relate to both traffic and stationary combustion sources.

We use Cox proportional hazards regression modeling to estimate the relationships between survival within the Veterans Cohort and each of these air pollutants, as well as various joint regressions with the traffic density measure used in previous analyses of this cohort.[7-9] The objective is to screen and compare plausible relationships.

DATA AND METHODS

Data

The Veterans Cohort Database. An earlier paper[6] presented initial Cox proportional hazard modeling results from a prospective study of all-cause mortality in this national cohort, initially comprising about 70,000 U.S. male military veterans who were diagnosed as hypertensive in the mid-1970s. This cohort had an average age at recruitment (in 1976) of 51 +/- 12 y; 35% are African-American and 81% had been smokers at some time. Non-pollution predictor variables in the baseline model include age, race, height, smoking (ever or at recruitment), age, systolic and diastolic blood pressure (BP), and body mass index (BMI). Interactions of BP and BMI with age are also considered. The study controls for socioeconomic status essentially by design because of the relative homogeneity of the cohort, but selected contextual variables on race, income, education, and climate, some of which were found to be significant predictors of survival, are also considered at the zip-code and county levels.

The database also includes county-level estimates of various indicators of ambient air quality, as well as of vehicular traffic density (VMTA), which is defined as annual vehicle-miles traveled per square mile of land area, in millions, based on data on vehicle-miles traveled (VMT) from EPA. Since the distribution of VMTA is approximately log-normal, we elected to use ln(VMTA) in Cox proportional hazards models of survival in some of the previous papers.[7-9] In this paper we consider both VMTA per se and its logarithm, as a means of examining the linearity of responses. All exposure data are considered at the county level, based on each subject's address at enrollment in the study (1975-6). Using county-level air quality data allows for exposures at other than the immediate residential location of the subject and admits the possibility of within-county residential relocation during the 26-y period of follow-up. However, these county-level estimates are based on simple averages of all fixed-point monitoring data in the county at various times and thus may not always be representative. We base subjects' implied exposures on estimated average conditions in their counties of residence at entry to the study.

Table 1 presents the descriptive statistics for the Veterans Cohort by mortality period and level of vehicular traffic density for 1985. As expected, the crude annual death rates increase over time as the cohort ages; there are only very minor differences in these rates between the full cohort and the subset restricted to higher levels of traffic density. Crude death rates are slightly lower in the more rural counties. About 66% of the cohort died through 2001. However, there are substantial differences in the VMTA data (about an order of magnitude); stratifying the cohort by traffic density and hence urbanicity also results in reduced ranges of the pollution variables (Table 2). We would expect such reductions to decrease statistical power in regression models.[15]

Vehicular Traffic Density. Data on annual vehicle-miles traveled (VMT) by county were obtained from the U.S. EPA for 1985, 1990, and 1997, for gasoline- and diesel-powered vehicles. Each was divided by the county land area, resulting in six measures of traffic density (VMTA). These six datasets are highly inter-correlated (R>0.99) and thus essentially interchangeable. The 1997 VMT data for gasoline-powered vehicles were used in previous analyses that emphasized the most recent mortality experience.[7-9] Because this paper focuses on the entire mortality follow-up period (1976-2001), we emphasize the 1985 traffic density data, which are about 30% smaller than the 1997 data. We also consider selected comparisons between analyses based on the 1985 or 1997 VMT data.

Stratification by Traffic Density. We consider all cohort subjects and two subsets, stratified by the county level of traffic density, cut at 7.39×10^6 veh-mi/mi^2. This arbitrary cut point is consistent with previous analyses of this cohort[9] and is the approximate mean of the 1997 distribution. Here we consider both 1985 and 1997 traffic density data. The risk estimates for all subjects portray the overall relationships, while comparing the results for high vs. low traffic densities is intended to test for thresholds in these relationships.

HAPS Data. The U.S. EPA has designated 188 substances as "hazardous" air pollutants (HAPS) under Section 112 of the Clean Air Act, for which sources are required to report their emissions as part of the "Toxics Release Inventory" (TRI). To provide national level risk assessments,[10,11] EPA used atmospheric dispersion modeling to estimate annual average ambient concentrations at county and census tract levels. This dispersion modeling is based on the frequency distributions of selected meteorological conditions.[11] Using 50th and 95th percentiles to represent county averages and hot-spot levels, respectively, we downloaded these ambient concentration estimates for 12 selected HAPS species:

1. Metals: arsenic, lead, manganese, mercury, nickel.
2. Traffic-related compounds: benzene, diesel particulate matter (DPM), formaldehyde, polycyclic organic materials (POM).
3. Others: chlorine, hydrochloric acid, polypropylene.
4. Coal combustion products include arsenic, mercury, and hydrochloric acid, in addition to the more traditional air pollutants discussed below.

Diesel particulate matter is not defined chemically and was designated as a "toxic air contaminant" in California in 1998,[16] according to Sexton et al.[17] According to an informal definition, DPM comprises elemental and organic carbon and trace amounts of sulfate, metals, and similar elements or compounds.[18] As discussed in on-line supplemental Appendix D, the ratio of DPM to elemental carbon is approximately 2.0

Descriptive statistics for the HAPS and traffic density variables are given in Table 2 (in ng/m^3). New York County (Manhattan), New York, has the highest vehicular traffic density in the United States; it also has the highest estimated concentrations of benzene, DPM, and formaldehyde (but not $PM_{2.5}$); the second highest levels of mercury, and the third highest level of polycyclic organic material. By contrast, the highest estimated levels of the selected metals, chlorine, and hydrochloric acid occur in rural counties and in West Virginia metropolitan areas.

AER National Estimates of Ambient Air Quality. These national estimates were produced by Atmospheric and Environmental Research, Inc., using the Community Multiscale Air Quality (CMAQ) modeling system with the MADRID aerosol algorithms and Advanced Plume Treatment (CMAQ-MADRID-APT). This state-of-the-science plume-in-grid air quality model was developed to provide a more realistic representation of the behavior of reactive plumes in the atmosphere within an Eulerian grid model framework.[12,13] This plume-in-grid model consists of a reactive plume model embedded into a three-dimensional grid-based model, CMAQ-MADRID, referred to as the host model. Annual average concentrations are based on hourly calculations at ground level.

Table 3 presents descriptive statistics of the ambient air quality estimates derived from the AER plume-in-grid air quality model.[13,19] They are based on EPA's 1999 inventory of the relevant emissions from both point and area sources; the model accounts for atmospheric chemical reactions and for long-term patterns in atmospheric dispersion. Annual estimates are obtained by summing hourly estimates. For these computations, AER uses a national grid of 36x36 km grid squares, which are generally smaller than most U.S. counties. Only the 48 contiguous states are included. To transform these outputs to the county level, we identified the latitude and longitude of the largest city within each county and the AER grid square that includes each of those locations. We then assigned the AER output concentration estimate at that location to the entire county. This provides estimates for 3065 counties that were then merged with the Veterans Cohort database, by subjects' county of residence at enrollment. Although assigning the county average to the largest city may entail exposure error in the less populous counties, it is unlikely that such errors would add substantially to the other exposure uncertainties, including the lack of personal exposure data and the existence of unquantified temporal trends.

The subject-weighted descriptive statistics are included in Table 2, along with unweighted statistics for all 3065 counties. The air quality indicators selected for this task include one species associated with large coal or oil combustion point sources (SO_4^{2-}), one associated with traffic (EC), and two associated with both area and point

sources (SO_2 and NO_x). Table 3 indicates that SO_2, NO_x, and EC are much more spatially variable than SO_4^{2-} and also shows that the initial distribution of subjects in this cohort captures the full range of national variation in the AER air quality data.

Appendix A in the On-Line Supplement identifies the counties with the highest levels of these four pollutants. New York City, Chicago, and some Louisiana locations have high levels of all four species. Most of the high-pollution counties are in the eastern half of the nation, where population and traffic densities are also higher.

Summary of Pollution Variables. This analysis considers 12 HAPS species, four AER variables, and either one or two traffic density variables (totaling either 17 or 18 pollution variables). 1985 VMT data comprise our base case, but we include 1997 VMT data for selected comparisons, especially when stratifying the cohort by traffic-density level. While we interpret the modeled ambient concentration data in this study as estimated exposures, they also represent indicators of residential proximity to emission sources. Pollutants with standard deviations greatly exceeding the mean (such as As or HCl) are sparsely distributed, resulting in lower probabilities of actual exposure. By contrast, our exposure paradigm is more reasonable for pollutants with more uniform spatial distributions like benzene or NO_x.

Bivariate Correlation Analysis. Table 4 presents the subject-weighted bivariate Pearson correlation coefficients among the pollutant variables used in this analysis. These correlations indicate the degree of independence of each species, which vary from essentially interchangeable (EC and NO_x) to moderately anti-correlated (Cl with SO_4^{2-} in high-density counties). Values above the unity diagonal in the matrix are for cohort subjects who resided in counties with lower than average 1985 traffic density; values below this diagonal are for subjects in the "high traffic-density" counties. Since most of these coefficients are statistically significant ($p < 0.05$) because of the large numbers of subjects involved, correlation coefficients of 0.7 or more are shown in boldface, as an arbitrary indicator of the stronger relationships. There are ten coefficients of 0.7 or larger for the low-density counties (above the diagonal) and eight for the high-density counties

(below the diagonal). The correlation matrix for all subjects is presented in the On-Line Supplement (Appendix A); these values tend to be stronger, because of the larger range of traffic-related pollutants, and there are 23 correlation coefficients of 0.70 or larger. Table 4 also shows the averages of between-pollutant correlations (excluding the unity values) at the bottom of the table. As expected, traffic-related pollutants are the most intercorrelated, especially in low-density counties. The least intercorrelated species are As, Cl, HCl, polypropylene, and sulfate (high-density counties). Correlation matrices based on the logarithms of pollutant concentrations are also presented in Appendix A.

The HAPS traffic indicators benzene, formaldehyde, and DPM and traffic density are more strongly correlated with EC and NO_x ($0.56 < R < 0.77$) in low-density counties than in high-density counties ($0.26 < R < 0.75$), perhaps because space-heating and industrial sources are relatively more important in dense urban areas. These traffic-related pollutants are only moderately correlated with SO_2 ($0.18 < R < 0.54$ in both high- and low-traffic counties, but SO_2 is more strongly correlated with EC and NO_x ($0.65 < R < 0.81$), regardless of traffic density, thus suggesting other common combustion sources such as space heating. Some studies of measured ambient air quality have noted summer morning peaks in SO_2,[20] local source effects stronger than.regional contributions,[21] and higher ambient concentrations near the ground, [22] all of which suggest SO_2 contributions from traffic, popular perceptions to the contrary not withstanding.

Bivariate correlations between pollutants may not always correspond with differences in their effects on mortality, as estimated by Cox proportional hazard regression. These Cox models include other contextual variables (like heating degree-days, for example) that are also correlated with air quality, but in ways that differ by pollutant. Such interactions between pollutants and contextual variables may result in differences between the bivariate relationships between pollutants and their mortality risk estimates.

Comparisons of these computed air quality estimates with measured values are presented and discussed in the On-Line Supplement (Appendix D). There are essentially two types of such comparisons: differences in mean values, and spatial correlations. In this

instance, spatial correlations are more relevant, because differences in mean values are accounted for in the effect estimates (discussed below). Correlations between predicted and measured air quality range from excellent for sulfates ($0.82 < R < 0.85$) to moderate for SO_2 and EC ($0.26 < R < 0.42$). This is consistent with the regional nature of sulfates and the local distributions of SO_2 and EC. NO_2 correlations are intermediate ($0.57 < R < 0.66$). The readily available comparisons for HAPS pollutants are those for metals in $PM_{2.5}$ Speciation Trends Network (STN)[7] and those presented by EPA.[23] EPA found good agreement between measured and modeled benzene, but the agreement between HAPS county-average model estimates and local STN metal measurements is poor. This could be due to temporal gradients (the STN data are for 2002) or because HAPS metal emissions are not necessarily in the particulate phase. However, there is reasonable agreement between the mean values for STN EC and HAPS DPM, taking into account the conversion factor of 2.0.[24] Overall, we find satisfactory agreement between key measured and modeled estimates of air quality parameters associate with vehicle emissions.

Methods

Regression Models. We consider five mortality follow-up periods (1976-81, 1982-88, 1989-96, 1997-2001, and 1976-2001) and three different subject selection criteria: unrestricted (all subjects), or restricted to those subjects who initially resided in counties for which 1985 traffic density was either greater or less than 7.39×10^6veh-mi/mi^2. For convenience, these Cox proportional hazard models were run without the interaction variables that were used in earlier papers,[6.8] since these variables were seen to have little effect on the pollution-survival relationships.[9] We consider each of the 18 pollutants separately, and we consider the HAPS and AER variables in two-pollutant models with 1985 traffic density.

We combined the results of the four sub-period analyses to provide alternative estimates of the mortality risks for each pollutant over the entire period. This was accomplished by computing a cumulative mortality risk (CMR) based on the risks estimated for each sub-period (i):

$$\ln(CMR) = \Sigma_i \ln(RR_i)D_i/\Sigma D_i \quad (1)$$

where RR_i is the risk for each sub-period and D_i is the number of cohort deaths during this period. There are four mortality sub-periods, as shown in Table 1. The standard error of each CMR was estimated by summing the variances of the relative risks for each sub-period, weighted by the deaths in each sub-period.

We also consider both the "raw" pollutant concentrations in these models and their logarithms, in part to examine the robustness of alternative specifications and also to consider whether the implied relationships might extend to very low concentration levels. This analysis is facilitated by the fact that the estimated minimal exposure levels are not limited by the minimum detection levels of typical ambient monitoring methods.

Measures of Effect. Making valid comparisons among disparate exposure measures requires dimensionless measures of effect, such as the *elasticity* (ε) metric often used by econometricians, in contrast to risks per unit of pollutant mass (such as per 10 ppb or 10 $\mu g/m^3$). Elasticity is defined as the percentage change in output resulting from a given percentage change in input.[25] It may also be thought of as the total percentage change in an effect attributed to a predictor variable, i.e., the *attributable risk* or "mean effect". When $\varepsilon = 1.0$, the relationship is directly proportional, when $\varepsilon = 0.10$, a 10% change in the predictor variable yields a 1% change in the endpoint, which is a more typical result for air pollution health effects. The regression coefficient of a log-log relationship is equivalent to the elasticity[25]; for a semi-log relationship, i.e., the log of health effects as a linear function of air quality levels, the elasticity or mean effect is obtained by multiplying the regression coefficient by the mean value of the pollutant.[25] The corresponding relative risks (RRs) are given by $\exp(\varepsilon)$. All relative risks in this paper are based on mean concentrations for relationships with linear exposures and elasticities for logarithmic relationships. This measure of effect is insensitive to uncertainties in the mean value of an independent variable; understating the mean will correspondingly inflate the regression coefficient, with no change in the elasticity.[25] The risks reported for

the logarithm of traffic density in previous papers[7,8] had different exposure bases, thus leading to higher risk estimates in some instances. We consider these effect estimates to be appropriate measures of puiblic health importance, within their 95% confidence intervals.

Timing of Exposures. Since traffic density is highly correlated over time among counties,[8] we used a common set of VMTA data for all mortality periods, as in previous analyses. We followed this protocol for all other pollutant variables as well. This is based on the hypothesis that the mean effect or elasticity will be less sensitive than the corresponding regression coefficient to changes in the mean value of the independent variable. This may be seen by comparing "effects" with "coefficients" in Tables 6 and 7 of the first Veterans Cohort paper.[6]

Measures of Model Fit. We use the Akaike Information Criterion (AIC) as a measure of overall model fit. Since AIC is proportional to the sample size, which varies by mortality follow-up period and dataset restriction, we use AIC/deaths (AICD) to compare fits among cohort subsets. We also compare the relative magnitudes of the standard errors of mean effects or elasticities among the various pollutants and subsets.

Sensitivity Analysis. The Cox proportional hazards analysis described above comprises 272 single-pollutant risk estimates and 128 two-pollutant risk estimates. As a sensitivity analysis and to consider possible effect modification, we used ordinary least squares regression to examine the variability within these sets of estimates, by timing of deaths, type of exposure model (linear vs. logarithmic), stratification by level of high-density, and pollutant species. This protocol provides more precise overall estimates of the differences among species and the effects of cohort subset parameters.

We also tested the hypothesis that the bivariate correlations among pollutants predict their relative rankings of risks,[15] after assigning one of them as the "true" predictor variable (P_t, with risk RR_t):

$$\ln(RR_j) = \mathbf{R_{t-j}} \ln(RR,) \quad (2)$$

where $\mathbf{R_{t-j}}$ is the subject-weighted correlation between pollutants *j* and *t*. This procedure is tested for several alternative choices of Pt and then ordinary least-squares regression is used to determine which of them appears to best fit the ensemble of RRs.

RESULTS

Single-Pollutant Regression Results

Proportional Hazards Models. We began the survival analysis by running proportional hazards models for each pollutant, one at a time, for each mortality sub-period and the overall mortality follow-up period (1976-2001). We compared linear and logarithmic (Appendix B) pollutant specifications and the effect of restricting the dataset by county traffic density level, cut at 7.39 x 10^6 veh-mi/mi^2. We computed relative mortality risks for each pollutant, model, and mortality follow-up sub-period; more than 700 Cox regression models were run in the course of this project. For brevity, we present only the aggregated cumulative risks based on linear exposures (Table 5). Risk estimates for each period and for logarithmic exposures (which are very similar to their linear counterparts) are available in Appendix B of the On-Line Supplement. The pollutants are listed in Table 5 in decreasing order of risk for all subjects.

Almost all of the CMR estimates in Table 5 indicate adverse effects (RR > 1), and 35 of the 54 risk estimates are statistically significant. The table also shows that the traffic-related pollutants benzene, formaldehyde, DPM, nitrogen oxides, and elemental carbon (EC) exhibit the highest CMR estimates for all subjects. However, DPM ranks further down the list when high-exposure counties are considered but is the most important pollutant in low-traffic counties. All pollutants are show statistically significant ($p<0.05$) mortality risks in the high-traffic subset, but the effects of manganese and sulfates are negative. Sulfate aerosol shows statistically significant negative risks in all counties considered. Comparing mortality risks between high and low traffic density subsets shows significant differences for benzene, formaldehyde, NOx, EC, and nickel, suggesting the presence of thresholds for these species.

The smaller risks attributed to known toxic agents like arsenic, chlorine, mercury, lead, or manganese, are also of interest. There are several possible reasons for these outcomes, including exposure errors associated with relatively sparsely distributed sources:

1. The "known" toxicity may relate to a relatively uncommon cause of death.
2. Toxicity may relate to a specific form of the agent, such as As(III) rather than As(V), or As particles rather than As vapor.
3. Toxicity may be dominated by a pathway other than inhalation, such as ingestion.
4. Thresholds may be involved, such that only a subset of cohort subjects were exposed to harmful levels. Such thresholds might become evident by stratifying the cohort by each of these pollutants separately instead of by traffic density.

Sensitivity Analyses. Linear regression analyses of the risk estimates that were used to construct Tables 5 and B-1 show the following, using dummy variables for each species to estimate overall differences in their risks (RRs) for all subjects and by level of 1985 traffic density (these results are similar to but do not exactly mirror those given in Table 5):

Mortality risks are significantly higher in counties with higher traffic densities (overall RR=1.07, for high-density relative to low-density).

For all subjects and exposure models, benzene, DPM, and formaldehyde have the highest mortality risks; NO_x and EC are next, and the risks for all other pollutants are significantly lower.

In the high-density counties, benzene has the highest risks; formaldehyde, NO_x, and EC are next; and all other pollutants (including DPM) have significantly lower risks.

Only DPM shows similar risks in both high and low traffic density counties.

There are only minor differences between the results based on linear exposure models shown in Table 5 and those based on logarithmic exposure models, shown in the on-line supplement (Table B-1).

The overall temporal trend in mortality risk is downward, at about one risk percentage point per decade (RR for 10 years = 0.99).

We also determined that mortality risks in the high-density counties account for the bulk of the risks in all counties, implying threshold effects. However, DPM and traffic density were exceptions, with significant mortality risks in the low-density counties as well.

To determine the role of (bivariate) correlations between pollutants in determining their relative mortality risks, we regressed mortality risks against pollutant inter-correlation coefficients. We assumed alternatively that either benzene, formaldehyde, EC, or NO_x is the true causal agent (P_t in Eq. 2) and that the risks attributed to all other pollutants are due to their correlations ($\mathbf{R_{t-j}}$) with this "true" agent P_t. We used OLS regression forced through the origin for this purpose. Most of these alternative results are very similar; thus, no significant differences could be discerned between benzene, formaldehyde, or NO_x as the most likely "true" agent. Figure 1 shows these relationships for benzene and NO_x.

In Figure 1(a), no pollutant has a mean effect higher than what might be expected from its correlation with benzene, while in Figure 1(b), benzene, formaldehyde, and DPM appear to show mean effects independent from NO_x. This suggests that benzene is the most important pollutant when all counties are considered together. However, when the high-density counties are considered separately, NO_x, benzene, EC, and formaldehyde (but not DPM) show at least some degree of independent effects. Pollutants not commonly associated with traffic, including SO_2, Ni, Hg, do not appear to exhibit independent effects in any of these cross-plots. However, SO_4^{2-} shows anomalously (and significantly) lower risks in Figures 1 (a, b, d), relative to what might have been expected

from its bivariate correlations. Each of the data points on Figures 1(c,d) is statistically significant, which indicates the wide range in precision of these risk estimates.

The data presentations of Figure 1 are also useful for making qualitative judgments about the relative importance of specific pollutants. Pollutant risks falling above the diagonal lines may be considered as "better" predictors than those below the line. Pollutant risks falling on the diagonal line may be considered as showing mainly surrogate relationships defined by their correlations with either benzene or NO_x.

Considerations of Model Fit. With respect to overall model fit, we found only minor variations in the Akaike Information Criteria (AIC) statistics according to the pollutant that was entered into a proportional hazards model with a given dataset. Because of the relatively large numbers of subjects, AICs typically comprise five or six digits, while differences in AICs among pollutants comprise only one or two digits. Among the various pollutants, there is little correspondence between the AICs and either pollutant effects or statistical significance, and only single-digit differences between AICs obtained with linear vs. logarithmic exposure models.

However, based on AICD values, we find substantially larger and systematic differences in model fits of up to 10% among mortality follow-up periods and subsets. The restricted datasets consistently fit better (lower AICDs) than their non-restricted counterparts, and there is a trend towards better fits with the most recent mortality follow-up periods. These findings lead to the conclusions that reducing the number of subjects considered may improve the overall model fit, and that overall model fit may not provide reliable guidance as to the most important pollutants.

As expected,[15] we also found a strong inverse log-log relationship between the standard errors of elasticities or of risk coefficients (based on mean concentrations) and the coefficients of variation (CV) of the pollutants (Figure 2). In this situation, statistical significance per se is not a measure of toxicity, since the *p*-level is affected by the large range in standard errors (more than an order of magnitude). This range is much larger

than the differences in standard errors between 26-yr and 4-yr follow-up periods, for example. Thus, statistical significance is necessary for a pollutant to be considered as an important predictor of survival, but significance level should not be used to rank relative importance to public health.

Two-Pollutant Models Including Traffic Density

Proportional Hazard Models. We used similar procedures with two-pollutant Cox models, comprising 1985 traffic density and each of the 16 other pollutants, one at a time (Table 6 and Figure 3). In each case, we computed the risk coefficient for the pollutant (mean effects or elasticities) and for traffic density, and then added them to provide an estimate of the combined effect of the pair (the "total" column in Table 6). For traffic-related pollutants, the combined effects are very similar to the single-pollutant effects, with traffic density making only minor contributions to the total effect. However, when combined with non-traffic related pollutants, the apparent relative risk of traffic density is about 1.03, which is similar to the results for traffic density alone and considerably less than Table 5 indicates for other traffic-related pollutants (RRs from 1.07 to 1.10). All of the "total" risk estimates are statistically significant, as are 14 of the 16 estimates of the traffic contribution, notwithstanding the modest levels in some cases. Similar results were obtained using logarithmic exposures (On-line Supplement Table B-2). Considering both linear and logarithmic exposures, the highest mortality risks are associated with benzene, DPM, NO_x,and formaldehyde, in combination with traffic density. The combination of sulfate aerosol and traffic density indicates the lowest mortality risks.

The right-hand section of Table 6 presents relative risks for the most recent mortality follow-up period (1997-2001), which is appropriate for estimating future mortality risks in this cohort. (A complete list of time-stratified risk estimates is presented in the On-Line Supplement, Table B-3.) Only three of these estimates are statistically significant, but benzene, formaldehyde, and DPM continue to be associated with the highest mortality risks. Lack of significance may have resulted in part from variance inflation

created by jointly regressing correlated pollutants, in addition to the reduced number of deaths during 1997-2001.

DISCUSSION

Summary of Findings

Much of the extant air pollution epidemiology literature focuses on specific "criteria" pollutants and the consideration of appropriate ambient air quality standards. This objective may be severely constrained by correlations among pollutants and by the realization that some of them may be serving mainly as markers for other, more toxic, agents. Uncertainty as to the true toxic agent(s) makes it more difficult to identify thresholds for use in setting ambient standards.[26] In this paper, we consider a suite of pollutants, including non-criteria species, in an attempt to focus more on source characteristics than on the individual pollutants or indicators used to regulate ambient air quality. Finding similar risks among groups of pollutants associated with a common emission source can add strength to the overall conclusions and provides a rational basis for pollution abatement. Risks associated with absolute concentration levels of specific pollutants may thus be less useful than identification of the most important sources.

We find that residence in counties with higher levels of traffic-related air pollutants shows stronger mortality risk estimates than those based on vehicular traffic density per se, and that each of these pollutants comprises the bulk of the risk in a joint regression with traffic density. These pollutants include gaseous species, some of which are indicated to pose larger mortality risks than most of the particulate species considered in this study. Mortality associations with benzene are among the strongest of these pollutants; our results indicate that benzene may be associated with about 10% of all-cause mortality in this cohort and 20% when limited to the counties with above-average traffic densities. This suggests that tailpipe or refueling emissions may be the most important environmental health aspects of vehicular traffic. In our previous studies of traffic density in combination with measured air quality,[8,9] we found that traffic density dominated, which suggests that the additional pollutant variables investigated here are also better predictors of cohort survival than locally measured ambient air quality

concentrations for criteria air pollutants. However, we have not evaluated possible contributions from brake or tire wear, road dust, or noise.

The finding of strong mortality risks associated with DPM in counties with lower traffic density (1985 mean = 2.7 x 10^6 veh-mi/mi^2) suggests that off-road diesel sources may also be important, assuming that off-road applications may be relatively more common in rural areas. It is not entirely clear how diesel ship emissions are handled in the NATA, but emissions of criteria pollutants from ships in port are considered as off-road mobile sources.

Tabulated national emissions inventory data (tons/yr) by source category[27] may help identify the important types of mobile sources. In the transport sector, volatile organic compounds (hydrocarbons) are emitted primarily from gasoline-powered vehicles. Total on-road NO_x emissions are almost double the off-road NO_x emissions. However, for diesel engines, on-road vehicles emit about 25% *less* total PM than off-road vehicles. This supports our finding of equivalent risks associated with DPM in both high- and low-traffic density counties and higher risks associated with NO_x and VOCs such as benzene in urban counties, because of the contributions of gasoline-powered vehicles and other urban sources.

This is the first American cohort mortality study to base estimated exposures of individual subjects on computed rather than measured ambient air quality levels. This protocol involves a trade-off between the reduced sample sizes and uncertainties imposed by relying on routine air quality monitoring networks and the larger sample sizes and implied combined uncertainties of estimated emission rates and complex atmospheric dispersion models. Because (non-differential) exposure error tends to bias regression results towards the null and to attenuate statistical significance,[26,28] our findings of substantial, precise, and internally consistent risk estimates were somewhat unexpected.

Potentially Critical Issues

Validity of Exposure Estimates. An important critical issue concerns the use of theoretical estimates of county-level exposures based on emissions rather than local ambient air quality measurements. We find that our exposure estimates are largely consistent with the ambient mobile-source HAPS data recently reported by the Health Effects Institute[29] and others.[30,31] NATA data have been used or cited in other analyses[32-34] and evaluated by EPA,[23] as discussed in on-line supplement Appendix D. However, mobile source emissions may be underestimated because of the difficulty in accounting for high-emitting vehicles that do not conform to regulatory models, especially in more recent years.[8]

In addition, comparisons of county averages with spot measurements are likely to be affected by local variability within counties.[23,30,31] The success of these regressions across a wide range of exposure levels derives in part from the fact that between-city variations in HAPS concentrations tend to be larger than within-city variations.[31]

Also, any errors stemming from differences between personal exposures and county-wide averages will tend to be less important for pollutants exhibiting large ranges in outdoor exposures. For example, a personal exposure uncertainty of say, 50% of the mean, would be more important for a pollutant like $PM_{2.5}$, having a range of a factor of 7,[7] than for pollutants such as DPM with a range of three orders of magnitude (Table 2), because of the much larger baseline variance of the latter. (Random error tends to attenuate a regression slope by a factor $R_{t\text{-}s}^2$, where $R_{t\text{-}s}$ is the correlation between the true exposure and the surrogate measure.[26]) This highlights the statistical advantage of working with source-specific pollutants that tend to produce wider ranges of estimated exposures than measured ambient concentrations that reflect the combined impacts of many types of sources.

However, there are also local "hot-spots" to consider, such as on-road exposures to vehicle exhaust[33-35] and benzene exposures from refueling operations.[36] The HAPS estimates are based on census tracts, which may reflect some of these hot-spots; we used the median concentration level for each county in the analysis, and we also downloaded

the 95th percentile levels. Hot-spot exposures may be an order of magnitude higher than the county averages considered here, but the relative rankings of urban vs. rural counties appear to be preserved, since the median and 95th percentiles of the HAPS data we used tend to be highly spatially correlated. Census tracts usually contain between 2500 and 8000 persons, so that their land areas vary inversely with population density and thus urbanicity. As a result, the more urban areas may have more precise concentration estimates than their rural counterparts in percentage terms, but not necessarily in absolute terms.

Notwithstanding these uncertainties in exposure estimates, we find consistent results using two different sets of emissions data and two very different dispersion models. This is shown, for example, by the strong correlation (R=0.75) between estimated DPM concentrations from NATA and estimated EC concentrations from AER (Tables A-2), notwithstanding non-traffic sources of EC. In addition, there are eight correlation coefficients of 0.8 or higher in Table A-2, indicating self-consistent spatial patterns in both NATA and AER data sets and between them. Our new risk estimates are also reasonably consistent with our previous estimates[7,8] based on measured air quality and with traffic density data that comprise a third independent database.

Timing Issues. The exposure data used here have been applied to various mortality periods, regardless of relative timing. This protocol may be problematic for exposures prior to the Clean Air Act of 1970 and does not accommodate subsequent vehicular emission reductions. For this cohort, we have no information on specific diseases involved in these deaths or their likely latency periods, and thus any associations with induction of new cases of chronic disease cannot be proven or disproven by this analysis. However, it is likely that at least some of the pollution-related deaths implied here may have also been affected by the much higher exposures that were likely experienced during previous decades.[29,37-40] This reinforces the need to consider trends in the mortality-pollution relationships during the 26-y period of follow-up (see Appendix Table B-3 in the On-Line Supplement). Such trends may also be affected by aging of thocohort and by differential survival of the hardiest subjects. Cook et al.[41] estimated

future levels of mobile-source air toxics and concluded that, while levels are projected to continue to decline, health concerns will likely remain.

Population Mobility.

All of our exposure estimates are based on the county of residence at enrollment in the study (1975-76). Although we also have the zip-codes of residence, we used counties in order to allow for non-residential (but reasonably local) exposures and the likelihood of within-county residential relocation during the follow-up period. As a means of assessing the potential consequences of residential mobility, we consulted U.S. Census data on migration (http://www.census/gov/population/www/cen2000/migration.html), based on a population sample of persons aged 65 and over. For the nation, 77.2% of the elderly population remained in the same residence from 1995 to 2000, and residential stability was slightly greater in the more urban states. During this period, 4.8% of the sample moved out-of-state (~1%/y), which leads to an estimate of 25% out-of-state movers over the 26-y period and the conclusion that population mobility is not likely to be a major issue with respect to our exposure estimates. Krewski et al.[3] reported a similar figure (18.5% movers) for the Six Cities study, which is based on much smaller residential areas. They also reported only minor effects of mobility on their mortality risk estimates.

Issues with Specific Pollutants and Mixtures.

Mobile source pollutants tend to be highly inter-correlated, such that their individual effects are difficult to separate. Nitrogen oxides have often been used as a marker for the mobile source mixture,[42] which provides no guidance as to which specific constituent(s) of the mixture should be regulated. For example, ultrafine particles are not monitored routinely and are not included in this analysis, but they tend to be correlated with NO_x in on-road exposures.[35] This quandary leads to the conclusion that epidemiology might be better served by considering all of the impacts from a source as a totality, rather than trying to develop dose-response relationships for each of the individual pollutants emitted. Noise and brake/tire/road dust effects are not specifically addressed in this analysis and thus cannot be ruled out as part of the overall traffic-related impact.

This analysis considers inhalation as the sole mode of exposure, while some of the HAPS we consider may have other modes, including ingestion and dermal absorption. Benzene, chlorine, arsenic, and lead are examples. If these modes of exposure are indeed important, the effects of inhalation presented here may be inflated, but to the extent that other exposure pathways are affected by local pollutant deposition, source proximity could still be a factor.

There are also indoor and personal inhalation exposures to consider for traffic-related pollutants, especially for benzene (cigarette smoking and cooking) and formaldehyde (building materials). Coke ovens are another important source of benzene. Charcoal cigarette filters tend to absorb benzene and other gases,[43] but a study of benzene biomarkers (e.g., muconic acid) showed that benzene uptake was related to smoking, occupation, time spent outdoors in urban areas, and time spent in vehicles.[44] Less information is available on formaldehyde biomarkers, but formaldehyde from mobile sources may be considered as just another component of the source-related mixture. Thus, for some pollutants, sources other than traffic may have contributed to the mortality risks estimated from these analyses.

While our results tend to emphasize mobile sources, there may also be concerns about mercury, arsenic, or nickel, which have been associated with large stationary sources burning residual fuel oil, coal, or municipal solid waste. Municipal incinerators are an important source of mercury emissions,[45,46] and urban excesses in wet deposition of mercury have been reported in Connecticut[46] and in the Chicago-Gary area.[47] Other studies have shown higher concentrations of Hg in gasoline than in diesel fuel[48-49] and still higher levels in liquefied petroleum gas (LPG).[50] Thus, the relatively strong correlations between airborne mercury and traffic pollutants seen in Table 4 may relate to both common sources and common urban locations of different types of sources. Nickel and arsenic have been identified in residual oil and coal fly ashes, respectively, but their relative toxicities and bioavailabilities (solubilities) vary according to the specific compounds involved.[51] Lipmann et al.[52] did not discuss specific nickel compounds and

noted that nickel was not always correlated with vanadium, as might be expected if the source were residual fuel oil.[53] Finally, although coal-fired power plants emit small quantities of metals in fly ash, they do not emit EC or polycyclic aromatic hydrocarbons.[54]

Our findings for sulfur compounds deserve special mention here, since we find consistent significant *positive* effects for sulfur dioxide (RR = 1.04 [1.02-1.05]) and statistically significant *negative* effects for sulfates (RR = 0.95 [0.92-0.97]), in spite of the relatively strong bivariate correlations between the two sulfur species. This is counter-intuitive from a toxicological perspective, since SO_2 is a reactive gas likely to be adsorbed in the upper airways or onto indoor structural surfaces, while sulfate particles are likely to enter the lower respiratory tract.[25] Such an assessment is also complicated by considering that sulfate particles tend to be water-soluble but that SO_2 may be adsorbed onto small insoluble particles that could be retained in the lung.[25] Our results indicate that the adverse effects indicated for SO_2 derive from its spatial correlations with traffic-related pollutants in the high-density counties, while the "beneficial" effects indicated for SO_4^{2-} stand alone in their own right, independently from other pollutants and regardless of traffic density (as shown in Figure 1). Several assessments[55-58] have determined that $(NH_4)_2SO_4$, the most likely ambient sulfate compound, is not a health hazard at current ambient levels, which is consistent with opinions reported by European experts.[59] Our negative findings for sulfates for this cohort are supported by previous negative results based on ambient measurements,[6,7] indicating that the previous negative findings were not the result of anomalous measurements. Survival plots of the raw data for high and low sulfate portions of the cohort also show an advantage for higher sulfate exposure, consistent with the proportional hazard model results that consider confounders. As seen in the On-Line Supplement (Table B-3), the risks for both sulfur oxide pollutants show negative trends over time, and neither is statistically significant for the 1997-2001 sub-period.

We did not include $PM_{2.5}$ in this analysis, in part because of the lack of appropriate data for all U.S. counties, and in part because $PM_{2.5}$ serves as an air quality *indicator* and is

not specific to any single emission source.[27] An analysis of hourly $PM_{2.5}$ concentrations at 20 monitoring stations around the New York City metropolitan area from 2000 to 2002 showed very smooth spatial and temporal distributions, because of the combined effects of local traffic and regional levels of secondary pollutants.[60] The overall average $PM_{2.5}$ level was about 12.5 $\mu g/m^3$, which meets the current annual NAAQS, even though portions of the New York area have the highest HAPS levels in the nation (Appendix A). The diurnal $PM_{2.5}$ data showed a sharp peak during morning rush hour, and mean levels were about 2 $\mu g/m^3$ higher on Thursdays than on Sundays, indicating relatively modest effects of traffic, on average. Our negative findings for sulfates would imply that the overall toxicity of PM mixtures containing sulfate should increase as the sulfate content declines over time, which has been reported by Jerrett et al.[2].

Measures of Effect. The risk estimates reported here are based on the mean concentrations of the pollutants in question, and thus could be interpreted as the public health benefit that would accrue if the pollutant in question were completely eliminated from the environment. However, putative irreducible background levels may be appreciable for some pollutants (25-30% of mean levels for benzene or formaldehyde, for example), but not for DPM. Thus, practical pollution abatement strategies may only be able to realize risk reductions comprising modest fractions of the estimates reported here. We also computed some risk estimates based on the 95th percentiles of the pollutant distributions, which resulted in only minor alterations of the rank orders in Table 5.

It is also important to realize that while statistical significance levels provide useful information on the reliability of a finding, significance level per se is not an appropriate indicator of the relative importance or toxicity of a pollutant. Thirty-five of the 54 risk estimates in Table 5 are significant, and there is no relationship between confidence interval width and level of risk. For example, chlorine is highly significant, not withstanding an excess risk level only about 10% of that of benzene, which is also statistically significant. This arises from differences in the spatial distributions of these pollutants, as seen from Figure 2 and by comparing standard deviations and mean values in Table 3. Chlorine is distributed very heterogeneously, with a spatial standard

deviation about five times its mean. By contrast, benzene is more homogeneous, with a standard deviation less than half its mean. This translates to an order of magnitude range in the coefficients of variation and thus in the standard errors of elasticities or mean effects[15] (Figure 2). There may indeed be an appreciable mortality risk associated with chlorine at its maximum concentration level (RR = ~1.16), but our analysis indicates that benzene effects reach this level of risk at many more locations than chlorine. Our analysis also suggests that the apparent national chlorine mortality risk may partly be due to its (spatial) correlation with traffic-related pollutants.

Analyses of Subsets. A previous paper[9] noted that mortality effects of traffic density summed over subsets of the follow-up period tend to exceed the effects estimated for the entire period. This is also the case with the pollutants under study here. We propose that this outcome results from temporal changes in the non-pollution risk factors in the model subsequent to enrollment in the study and differences in the resulting confounding. However, the phenomenon generally does not occur here with subsets by traffic density; the sums of high- and low-density traffic effects are very nearly equal to those for all subjects. This supports the hypothesis that risk factor changes during follow-up can be important in estimating the overall pollution risks appropriately and suggests the presence of confounding.

The major differences in mortality risks seen here between sets of counties with high and low traffic densities suggest that thresholds may exist for some pollutants. Thus, caution is warranted in trying to estimate risks for the entire nation based on ambient data obtained from urban counties.

Comparisons with Other Risk Estimates

Comparisons with Previous Estimates for This Cohort. The first publication[6] on air pollution risks for this cohort presented mean pollution risks in terms of matrices of mortality sub-periods by pollution measurement periods (Table 7 of that paper, for deaths through 1996). We found it difficult to discern a consistent pattern in the timing of responses vs. those of exposures, in part because of high temporal correlations among the

air quality measures. Below we compare the estimates from previous papers with those of the present analysis, using mean effect ranges and standard errors, for brevity. Table 7A compares the present results with those of the first Veterans Cohort paper,[6] by mortality follow-up period. Table 7B compares the present results for the 1997-2001 period with those obtained using data on $PM_{2.5}$ constituents from EPA's Speciation Trends Network.[7] None of the differences between estimates based on measurements vs. modeling is statistically significant, and the relative rankings of pollutants are similar for the two sets of risk estimates. Also, note in Table 7B that the standard errors of the modeled estimates tend to be smaller than those based on measured air quality. In this sense, the modeled estimates should be considered "better" predictors of survival in this cohort.

Comparisons with Previous Risk Assessments. Woodruff et al.[61] estimated 1990 ambient levels of HAPS for all of the census tracts in the contiguous United States and compared them with EPA "benchmark" levels, including those for a cancer risk of 10^{-6}. They concluded that levels of benzene and formaldehyde may have posed excess risks by this definition, but that arsenic and nickel did not.

Wu and Pratt[62] analyzed 1996 HAPS levels in Minnesota, considering both emission levels and toxicity rankings. Their rankings of the 12 HAPS considered here include formaldehyde (#2), nickel (#3), manganese (#4), benzene (#10), and lead (#13).

Sexton et al.[17] performed a similar assessment for the Houston area, basing "benchmark" levels on the judgments of a panel of experts. Ozone and $PM_{2.5}$ were also included, based on exceedances of NAAQS levels, in addition to 1999 HAPS levels. They concluded that O_3, $PM_{2.5}$, DPM, benzene, formaldehyde, and chlorine (among others) posed "definite" risks in Houston, and that arsenic compounds were a "possible" risk. This area is of interest here because our initial analysis of the Veterans cohort[6] identified Houston as a relatively high-mortality location.

Appendix C in the On-Line Supplement compares our results for associations between total mortality and ambient air quality with those of previous long-term studies from the literature.

Support from Toxicology

The inability to identify the individual contributions of correlated pollutants has often been a limitation of epidemiology. Toxicology experiments with controlled exposures on animals or *in vitro* may thus offer assistance. However, findings of experiments with specific types of particles have been mixed and often require compromised subjects in order to show effects;[63-67] testing with actual source emissions may be more promising. These include exposures on[68] and near[69] roadways and to diluted engine exhaust.[70-72] Engine exhaust experiments with particles removed by filtering show risks associated with gaseous constituents as well.[71] Experiments with concentrated ambient PM often show effects with crustal materials[73-76] that might implicate road dust, the effects of which were not evaluated in this study.

CONCLUSIONS

We conclude that survival of members of the Washington University-EPRI Veterans Cohort is strongly and robustly associated with county-average levels of traffic-related air pollution, as estimated by several protocols, based on residence at entry to the study. Both gaseous and particulate species are implicated, including hazardous air pollutants; sources of these pollutants other than traffic may also be implicated. The mortality risks in this cohort appear to be declining slightly over time, and the overall composition of traffic emissions has changed with the imposition of engine exhaust control systems. Except for DPM, mortality relationships are stronger in the counties with higher levels of traffic density. These findings are supported by other risk assessments and epidemiological studies of the health effects of traffic in North America and Europe, in addition to toxicological experiments. However, health effects of vehicular traffic may also involve degradation products from vehicle or roadway wear, traffic noise, stress, or socioeconomic effects associated with preferred residential locations. While this study effectively controls for socioeconomic status by design, we have not specifically evaluated these other factors.

We also conclude that statistical significance alone is not an appropriate indicator of the importance (i.e., toxicity) of a pollutant predictor variable. Significant excess risks as low as 0.5% were detected for some pollutants. In counties with high levels of vehicular traffic density, all of the pollution variables considered here show statistically significant relationships with mortality; inter-pollutant correlations may explain many of these relationships. Emission sources located in densely populated areas appear to be the common factor. We are unable to identify specific pollutants that might be uniquely responsible for the observed excess mortality, and we recommend extension of these analytical and modeling techniques to other cohorts, to further test the hypotheses generated here.

We find the following specific conclusions with respect to predicting survival in this cohort, based on modeled county-level estimates of residential exposures:

> Selected traffic-related air pollutants (benzene, formaldehyde, diesel particulate, oxides of nitrogen, elemental carbon) are better predictors than traffic density per se (Figure 1[a,b]).
>
> The AER-modeled EC and NO_x exposures are better predictors than the measured air quality values used previously, as shown by the more precise risk estimates achieved with modeling (Table 7B).
>
> Significant mortality risks associated with SO_2 are limited to high-traffic density counties (Table 5), where SO_2 appears to be a surrogate variable (Figure 1).
>
> Among the potentially toxic trace elements in fossil fuels or emitted from metal-working industries (As, Hg, Mn, Ni, Pb), Ni appears to be the most important in high-traffic counties, but Ni also appears to be a surrogate variable (Figure 1). Risks for As, Hg, Mn, and Pb are significantly lower, in all counties (Table 5)

Other non-metal HAPS not related to either traffic or combustion (chlorine, hydrochloric acid, polypropylene) are not significant independent predictors of survival in the total cohort (Figure 1).

The negative sulfate risk coefficients previously reported on the basis of ambient measurements in selected counties are confirmed with nationwide modeled estimates (Tables 5, 6, 7).

Traffic density and ambient concentrations of related pollutants tend to be higher in the more densely populated cities of the Northeast, where residual fuel oil containing nickel and sulfur is commonly used.[52] These considerations lead to the conclusion that cities can be important sources of a variety of air pollutants besides those directly emitted in vehicle exhaust. Air pollution epidemiology studies should consider a suite of potentially causal agents before focusing on any one of them, including non-criteria and hazardous species.

ACKNOWLEDGEMENTS

The Veterans Cohort database is maintained at Washington University, St. Louis, School of Medicine, under the leadership of J. Philip Miller; the proportional hazards modeling was done there by Jack Baty. The Electric Power Research Institute funded the bulk of this study but the authors are solely responsible for these findings. We thank Atmospheric and Environmental Research, Inc., for their dispersion modeling work, Sheldon Lipsky for assistance in downloading the EPA HAPS data, and three anonymous reviewers for their helpful suggestions.

REFERENCES

1. Pope, C.A. III, Thun, M.J., Namboodiri, M.M., Dockery, D.W., Evans, J.S., Speizer, F.E., Heath, C.W., Jr. Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults; *Am J Respir Crit Care Med.* **1995**, *151*, 669-674.

2. Jerrett, M., Newbold. K.B., Burnett, R.T., Thurston, G., Lall, R., Pope, C.A. III, Ma, R., De Luca, P., Thun, M., Calle, J., Krewski, D. Geographies of uncertainty in the

health benefits of air quality improvements; *Stoch Environ Res Risk Assess* . **2007**, *21*, 511-522.

3. Krewski, D., Burnett, R.T., Goldberg, M.S., Hoover, K., Siemiatycki, J., Abrahamowicz, M., White, W.H., others. 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 Institute, **2000**. Part I. Replication and Validation (http://www.healtheffects.org/Pubs/Rean-part1.pdf) and Part II. Sensitivity Analyses (http://www.healtheffects.org/Pubs/Rean-part2.pdf).

4. Jerrett, M., Burnett, R.T., Ma, R., Pope, C.A. 3rd, Krewski, D., Newbold, K.B., Thurston, G., Shi, Y., Finkelstein, N., Calle, E.E., Thun, M.J.. Spatial analysis of air pollution and mortality in Los Angeles; *Epidemiology*. **2005**, *16*, 727-736.

5. Jerrett, M., Burnett, R., Ma, R., Pope, C.A. III, Thun, M., Calle, J., Thurston, G., Ito, K., Ross, Z., Krewski, D. Air pollution and mortality in New York City. Poster presented at the Annual Meeting of the Health Effects Institute, San Francisco, April **2006**. Also see presentation by Krewski et al. at www.healtheffects.org/Slides/AnnualConference/2008/Krewski.pdf (accessed Nov. 5, 2008).

6. Lipfert, F.W., Perry, H.M. Jr., Miller, J.P., Baty, J.D., Wyzga, R.E., Carmody, S.E.. The Washington Unversity-EPRI Veterans Cohort Mortality Study: preliminary results; *Inhal Toxicol.* **2000,** *12*, *Suppl 4*, 41-73.

7. Lipfert, F.W., Baty, J.D., Miller, J.P., Wyzga, R.E.. $PM_{2.5}$ constituents and related air quality variables as predictors of survival in a cohort of U.S. military veterans; *Inhal Toxicol.* **2006,** *18*, 645-657.

8. Lipfert, F.W., Wyzga ,R.E., Baty, J.D., Miller, J.P. Traffic density as a surrogate measure of environmental exposures in studies of air pollution health effects: Long-term mortality in a cohort of US veterans; *Atmos Environ.* **2006**, *40*, 154-169.

9. Lipfert FW, Wyzga RE, Baty JD, Miller JP. Vehicular traffic effects on survival within the Washington University-EPRI veterans cohort: new estimates and sensitivity studies. Inhal Toxicol. 2008 Aug;20(10):949-60.

10. U.S. Environmental Protection Agency, 1996 National Air Toxics Assessment, http://www.epa.gov/ttn/atw/nata; U.S. Environmental Protection Agency, 1999 National Air Toxics Assessment, http://www.epa.gov/ttn/atw/nata1999/.

11. Rosenbaum, A.S., Axelrad, D.A., Woodruff, T.J., Wei, Y-H., Ligocki, M.P., Cohen, J.P., National estimates of outdoor air toxics concentrations; *J Air Waste Manag Assoc.* **1999,** *49*, 1138-1152.

12. Karamchandani, P.K., Vijayaraghavan, K., Seigneur, C., CMAQ-MADRID-APT Version 4.5.1 User's Guide; **2006**, EPRI, Palo Alto, CA.

13. Karamchandani, P., Vijayaraghavan, K., Chen, S-Y., Seigneur, C., Edgerton ,E.S., Plume-in-grid modeling for particulate matter; *Atmos Environ*. **2006,** *40*, 7280-7297.

14. Pun, B.K., Seigneur, C., Bailey, E.M., Gautney, L.L., Douglas, S.G., Haney, J.L., Kumar, N. Response of atmospheric particulate matter to changes in precursor emissions: A comparison of three air quality models; *Enviro Sci Tech*, in press.

15. Lipfert, F.W., Wyzga, R.E., Statistical Considerations in Determining the Health Significance of Constituents of Airborne Particulate Matter; *J Air Waste Manag Assoc.* ***1999,*** *49 (special issue)*, 182-189.

16. California Air Resources Board, The Toxic Air Contamination Identification Process: Toxic Air Contaminants from Diesel-Fueled Engines, Fact Sheet. http://www.arb.ca.gov/toxics/dieseltac/factsht1.pdf.

17. Sexton, K., Linder, S.H., Marko, D., Bethel, H., Lupo, P.J., Comparative assessment of air pollution-related health risks in Houston; *Environ Health Perspect.* **2007,** 115, 1388-1393.

18. Somers J, personal communication, Nov. 14, 2007.

19. Vijayaraghavan, K., Karamchandani, P., Seigneur, C., Plume-in-grid modeling of summer air pollution in Central California; *Atmos Environ*. **2006,** *40*, 5097-5109.

20. Rattigan OV, Hogefe O, Felton HD et al., Multi-year urban and rural semi-continuous $PM_{2.5}$ sulfate and nitrate measurements in New York state: Evaluation and comparison with filter based measurements, *Atmos Environ* **2006,** *40, Suppl 2*, 192-205.

21. Bari A, Dutkiewicz VA, Judd CD et al., Regional sources of particulate sulfate, SO_2, $PM_{2.5}$, HCl, and HNO_3, in New York, NY. *Atmos Environ* **2003,** *37*, 2837-44. Also see Wheeler AJ, Smith-Doiron M, Xu Xiaohong, Gilbert NL, Brook JR. Intra-urban variability of air pollution in Windsor, Ontario – Measurement and modeling for human exposure assessment. *Environ Res* **2008,** *106*, 7-16.

22. Restrepo C, Zimmerman R Thurston G et al., A comparison of ground-level air quality data with New York State Department of Environmental Conservation monitoring stations in South Bronx, New York. *Atmos Environ* **2004,** *38*, 5295-04.

23. http://www.epa.gov/ttn/atw/nata/mtom_pre.html (summary); http://www.epa.gov/ttn/atw/nata/draft6.html (complete report). Last updated Aug. 4, 2008. Accessed Aug. 13, 2008.

24. ICF Consulting, DPM Model-To-Measurement Comparison, Report EPA 420-D-02-004, October 2002.

25. Lipfert, F.W., *Air Pollution and Community Health*; van Nostrand (Wiley): New York, 1994. pp. 71-73.

26. Lipfert, F.W., Wyzga, R.E., Effects of Exposure Error on Environmental Epidemiology, Proc. International Symposium on the Health Effects of Particulate Matter, Prague. AWMA Publ. VIP-80, pp. 155-166 (**1998**). Also see Lipfert, F.W., The Use and Misuse of Surrogate Variables in Environmental Epidemiology, *J. Environmental Medicine* **1999**, *1*, 267-278.

27. U.S. Environmental Protection Agency,National Air Quality and Emission Trends Report, 1999. Report EPA 454/R-01-004, March **2001**. Appendix A.

28. Mallick, R., Fung, K., Krewski, D. Adjusting for measurement error in the Cox proportional hazards regression model; *J Cancer Epidemiol Prev*. **2002**, *7*, 155-164.

29. HEI Air Toxics Review Panel, Mobile-Source Air Toxics: A Critical Review of the Literature on Exposure and Health Effects. HEI Special Report 16, **2007**. Health Effects Institute, Boston, MA.

30. Touma, J.S., Cox, W.M., Tikvart, J.A., Spatial and temporal variability of ambient air toxics data; *J Air Waste Manag Assoc.* **2006,** *56*,1716-1725.

31. Baker, A.K., Beyersdorf, A.J., Doezema, L.A., Katzenstein, A., Meinardi, S., Simpson, I.J., Blake, D.R., Rowland, F.S. Measurements of nonmethane hydrocarbons in 28 United States cities; *Atmos Environ.* **2008**, *42*, 170-182.

32. Marshall JD, Teoh S-K, Nzaroff WW. Intake fraction of nonreactive vehicle emissions in US urban areas. *Atmos Environ* **2005,** *39*, 1363-71.

33. Greco SL, Wildon AM, Spengler JD, Levy JI, Spatial patterns of mobile source particulate matter emissions-to-exposure relationships across the United States. *Atmos Environ* **2007**, 41, 1011-25.

34. Ozkaynak, H., Palma, T., Touma, J.S., Thurman, J.. Modeling population exposures to outdoor sources of hazardous air pollutants; *J Expo Sci Environ Epidem.* **2008,** *18*, 45-58.

35. Fruin, S., Westerdahl, D., Sax, T., Sioutas, C., Fine, P.M., Measurements and predictors of on-road ultrafine particle concentrations and associated pollutants in Los Angeles; *Atmos Environ*. **2008**, *42*, 207-219.

36. Karakitsios, S.P., Papaloukas, C.L., Kassomenos, P.A., Pilidis, G.A. Assessment and prediction of exposure to benzene of filling station employees; *Atmos Environ.* **2007**, *41*, 9555-9569.

37. Edgerton, S.A., Holdren, M.W., Smith, D.L., Shah, J.J., Inter-urban comparison of ambient volatile organic compound concentrations in U.S. cities; *J. Air Poll Control Assoc.* **1989,** *39*, 729-732.

38. Ban-Weiss, G.A., McLaughlin, J.P., Harley, R.A., Lunden, M.M., Kirchstetter, T.W., Kean, A.J., Strawa, A.W., Stevenson, E.D., Kendall, G.R., Long-term changes in emissions of nitrogen oxides and particulate matter from on-road gasoline and diesel engines; *Atmos Environ.* **2008,** *42*, 220-232.

39. Louchouarn, P., Chillrud, S.N., Houel, S., Yan, B., Chaky, D., Rumpel, C., Largeau, C., Bardoux, G., Walsh, D., Bopp, R.F. Elemental and molecular evidence of soot- and char-derived black carbon inputs to New York City's atmosphere during the 20th century; *Environ Sci Tech,* **2007**, *41*, 82-87.

40. Wakeham, S.G., Forrest, J,, Masiello, C.A., Gelinas, Y., Alexander, C.R., Leavitt, P.R. Hydrocarbons in Lake Washington sediments. A 25-year retrospective in an urban lake; *Environ Sci Tech.* **2004**, *38*, 431-439.

41. Cook, R., Strum, M., Touma, J.S., Palma, T., Thurman, J., Ensley, D., Smith, R. Inhalation exposure and risk from mobile source air toxics in future years; *J Expo Sci Environ Epidem.* **2007,** *17*, 95-105.

42. Beckerman, B., Jerrett, M., Brook, J.R., Verma, D.K., Arain, M.A., Finkelstein, M.M. Correlation of nitrogen dioxide with other traffic pollutants near a major expressway; *Atmos Environ.* **2008**, *42*, 275-290.

43. Scherer, G., Urban, M., Engl, J., Hagedorn, H.W., Riedel, K., Influence of smoking charcoal filter tipped cigarettes on various biomarkers of exposure; *Inhal Toxicol.* **2006**, *18*, :821-829.

44. Berthoin, K., Broekaert, F., Robin, M., Haufroid, V., De Burbere, C., Bernard, A. Serum pneumoproteins and biomarkers of exposure to urban air pollution: a cross-sectional comparison of policemen and foresters; *Biomarkers* **2004**, *9*, 341-352.

45. Glass, G.E., Sorensen, J.A., Schemidt, K.W., Rapp, G.R. Jr. New source identification of mercury contamination in the Great Lakes; *Environ Sci Tech.* **1990,** *24*, 1059-1069.

46. Nadim, F., Perkins, C., Liu, S., Carley, R.J., Hoag, G.E. Long-term investigation of atmospheric mercury contamination in Connecticut; *Chemosphere* **2001,** *45*, 1033-1043.

47. Landis, M.S., Vette, A.F., Keeler, G.J. Atmospheric mercury in the Lake Michigan basin: Influence of the Chicago/Gary urban area; *Environ Sci Tech.* **2002**, *36*, 4508-4517.

48. Landis, M.S., Lewis, C.W., Stevens, R.K., Keeler, G.J., Dvonch, J.T., Tremblay, R.T., Ft. McHenry tunnel study: Source profiles and mercury emissions from diesel and gasoline powered vehicles; *Atmos Environ*. **2007**, *41*, 8711-8724.

49. Wilhelm, S.M., Kirchgessner, D.. Mercury in U.S. crude oil: A study by U.S. EPA, API, and NPRA; *Society of Petroleum Engineers Paper SPE 80573*, **2003**.

50. Won, J.H., Park, J.Y., Lee, T.G., Mercury emissions from automobiles using gasoline, diesel, and LPG; *Atmos Environ*. **2007**, *41*, 7547-7552.

51. Huggins, F.E., Huffman, G.P., Linak, W.P., Miller, C.A., Quantifying hazardous species in particulate matter derived from fossil-fuel combustion; *Environ Sci Tech.* **2004**, *38*, 1836-1842.

52. Lippmann, M., Ito, K., Hwang, J-S., Maciejczyk, P., Chen, L-C. Cardiovscular effects of nickel in ambient air; *Environ Health Perspect.* **2006**, *114*, 1662-1669.

53. Okuda, T., Nakao, S., Katsuno, M., Tanaka, S., Source identification of nickel in TSP and $PM_{2.5}$ in Tokyo, Japan; *Atmos Environ.* **2007,** *41*, 7642-7668.

54. Meij, R., te Winkel, H., The emissions of heavy metals and persistent organic pollutants from modern coal-fired power stations, *Atmos Environ.* **2007**, *41*, 9262-9272.

55. Schlesinger, R.B., Kunzli, N., Hidy, G.M., Gotschi, T., Jerrett, M. The health relevance of ambient particulate matter characteristics: coherence of toxicological and epidemiological inferences; *Inhal Toxicol.* **2006,** *18*, 95-125.

56. Grahame, T., Schlesinger, R. Evaluating the health risk from secondary sulfates in eastern North American regional ambient air particulate matter; *Inhal Toxicol*. **2005**, *17*, 15-27.

57. Schlesinger, R.B., Cassee, F. Atmospheric secondary inorganic particulate matter: the toxicological perspective as a basis for health effects risk assessment; *Inhal Toxicol*. **2003,** *15*, 197-235.

58. Schlesinger, R.B. The health impact of common inorganic components of fine particulate matter ($PM_{2.5}$) in ambient air: a critical review; *Inhal Toxicol* . **2007**, *19***,** 811-832.

59. Cooke, R.M., Wilson, A.M., Tuomisto, J.T., Moarales, O., Taino, M., Evans, J.S. A probabilistic characterization of the relationship between fine particulate matter and mortality: Elicitation of European Experts; *Environ Sci Technol.* **2007**, *41*, 6598-6605.

60. DeGaetano, A.T., Doherty, O.M., Temporal, spatial and meteorological variations in hourly $PM_{2.}5$ concentration extremes in New York City; *Atmos Environ.* **2004,** *38*, 1547-1558.

61. Woodruff, T.J., Axelrad, D.A., Caldwell, J., Morello-Frosch, R., Rosenbaum, A. Public health implications of 1990 air toxics concentrations across the United States; *Environ Health Perspect.* **1998**, *106*, 245-251.

62. Wu, C.Y., Pratt, G.C., Analysis of air toxics emission inventory: Inhalation toxicity-based ranking; *J Air Waste Manag Assoc.* **2001,** *51*, 1129-1141.

63. Ayres JG, Borm P, Cassee FR, Castranova V, Donaldson K, Ghio A, Harrison RM, Hider R, Kelly F, Kooter IM, Marano F, Maynard RL, Mudway I, Nel A, Sioutas C, Smith S, Baeza-Squiban A, Cho A, Duggan S, Froines J. Evaluating the toxicity of airborne particulate matter and nanoparticles by measuring oxidative stress potential--a workshop report and consensus statement. *Inhal Toxicol*. **2008**, *20*, 75-99.

64. Borm PJ, Kelly F, Kunzli N, Schins RP, Donaldson K. Oxidant generation by particulate matter: from biologically effective dose to a promising, novel metric. *Occup Environ Med.* **2007**, *64*, 73-4.

65. 13. Chang CC, Hwang JS, Chan CC, Cheng TJ. Interaction effects of ultrafine carbon black with iron and nickel on heart rate variability in spontaneously hypertensive rats. *Environ Health Perspect.* **2007**, *115*, 1012-7.

66. 14. Chen LC, Hwang JS. Effects of subchronic exposures to concentrated ambient particles (CAPs) in mice. IV. Characterization of acute and chronic effects of ambient air fine particulate matter exposures on heart-rate variability. *Inhal Toxicol.* **2005**, *17*, 209-16.

67. Schwarze PE, Ovrevik J, Lag M, Refsnes M, Nafstad P, Hetland RB, Dybing E. Particulate matter properties and health effects: consistency of epidemiological and toxicological studies. *Hum Exp Toxicol.* **2006**, *25*, 559-79.

68. Elder A, Gelein R, Finkelstein J, Phipps R, Frampton M, Utell M, Kittelson DB, Watts WF, Hopke P, Jeong CH, Kim E, Liu W, Zhao W, Zhuo L, Vincent R, Kumarathasan P, Oberdorster G. On-road exposure to highway aerosols. 2. Exposures of aged, compromised rats. *Inhal Toxicol.* **2004**, *16 Suppl 1*, 41-53.

69. Kleinman MT, Hamade A, Meacher D, Oldham M, Sioutas C, Chakrabarti B, Stram D, Froines JR, Cho AK. Inhalation of concentrated ambient particulate matter near a heavily trafficked road stimulates antigen-induced airway responses in mice. *J Air Waste Manag Assoc.* **2005**, *55*, 1277-88.

70. Campen MJ, McDonald JD, Gigliotti AP, Seilkop SK, Reed MD, Benson JM. Cardiovascular effects of inhaled diesel exhaust in spontaneously hypertensive rats. *Cardiovasc Toxicol.* **2003**, *3*, 353-61.

71. Campen MJ, Babu NS, Helms GA, Pett S, Wernly J, Mehran R, McDonald JD. Nonparticulate components of diesel exhaust promote constriction in coronary arteries from ApoE-/- mice. *Toxicol Sci.* **2005**, *88*, 95-102.

72. Lund AK, Knuckles TL, Obot Akata C, Shohet R, McDonald JD, Gigliotti A, Seagrave JC, Campen MJ. Gasoline exhaust emissions induce vascular remodeling pathways involved in atherosclerosis. *Toxicol Sci.* **2007**, *95,* 485-94.

73. Wellenius GA, Coull BA, Godleski JJ, Koutrakis P, Okabe K, Savage ST, Lawrence JE, Murthy GG, Verrier RL. Inhalation of concentrated ambient air particles exacerbates myocardial ischemia in conscious dogs. *Environ Health Perspect.* **2003**, *111,* 402-8.

74. Steerenberg PA, van Amelsvoort L, Lovik M, Hetland RB, Alberg T, Halatek T, Bloemen HJ, Rydzynski K, Swaen G, Schwarze P, Dybing E, Cassee FR. Relation between sources of particulate air pollution and biological effect parameters in samples from four European cities: an exploratory study. *Inhal Toxicol.* **2006**, *18,* 333-46.

75. Ovrevik J, Myran T, Refsnes M, Lag M, Becher R, Hetland RB, Schwarze PE. Mineral particles of varying composition induce differential chemokine release from epithelial lung cells: Importance of physico-chemical characteristics. *Ann Occup Hyg* **2005,** *49,* 219-31.

76. Chang CC, Hwang JS, Chan CC, Wang PY, Cheng TJ. Effects of concentrated ambient particles on heart rate, blood pressure, and cardiac contractility in spontaneously hypertensive rats during a dust storm event. *Inhal Toxicol.* **2007**, *19,* 973-8.

Table 1 Descriptive Statistics for the EPRI-Washington University Veterans Cohort Study

period	live subjects	deaths	average annual death rate	traffic density (VMTA) mean	std dev
A. All subjects					
1976-01	67938	44653	0.0253	12.17	15.3
1976-81	67938	11938	0.0293		
1982-88.	56000	13885	0.0354		
1989-96	42115	13119	0.0389		
1997-01	28996	5711	0.0394		
B. Restricted to subjects in counties with traffic density > 7.39 x 10^6 veh-mi/mi^2					
1976-01	29808	19666	0.0254	24.3	16.2
1976-81	29808	5240	0.0293		
1982-88.	24568	6133	0.0357		
1989-96	18435	5760	0.0391		
1997-01	12675	2533	0.0400		
C. Restricted to subjects in counties with traffic density <= 7.39 x 10^6 veh-mi/mi^2					
1976-01	38130	24987	0.0252	2.69	2.38
1976-81	38130	6698	0.0293		
1982-88.	31432	7752	0.0352		
1989-96	23680	7359	0.0388		
1997-01	16321	3178	0.0389		

Table 2 Descriptive Statistics of selected HAPS and traffic density data (county median concentrations, ng/m^3)

	---------- all subjects ----------						restricted to traffic density > 7.39	
	(n = 3065 counties)				(n = 67938 subjects)		(n = 29808 subjects)	
species	**mean**	**std dev**	**min**	**max**	**weighted mean**	**weighted s dev**	**wtd mean**	**wtd s dev**
arsenic	0.06	0.44	0	18	0.152	0.358	0.20	0.23
benzene	760	335	481	4760	1520	605	1990	475.
chlorine	5.73	56.5	0	2769	19.1	98.9	16.8	31.4
diesel PM	779	697	15	15100	1810.	999.	2534	897
formaldehyde	547	370	251	6810	1155	587	1623	522
hydrochloric acid	111	573	0	14637	168	321	218	157
local mercury	0.11	0.61	0	28	0.57	0.62	1.02	0.61
lead	1.05	4.05	0	141	5.68	7.31	8.63	6.89
manganese	1.25	5.89	0	238	3.08	3.79	4.13	3.56
nickel	0.46	1.49	0	57	2.09	1.87	3.49	1.67
polycyclic organics	24.5	39.5	0.0	618	96.4	83.8	148	94/7
polypropylene	0.17	0.96	0	12.4	0.183	1.00	0.34	1.48
1997 traffic density	1.72	9.6	0.004	265	17.11	20.7	34.1	21.5
1985 traffic density	1.23	6.87	0.003	183	12.17	15.3	24.3	16. 2

Table 3 Descriptive Statistics for the AER Ambient Air Quality Concentration Estimates

Species	Raw Data		Subject-Weighted Data				Minimum	Maximum
			all subjects		high traffic counties			
	mean	std dev	mean	std dev	mean	std dev		
SO_2 (ppb)	1.86	1.76	4.28	3.12	6.37	3.16	0.06	19.2
NO_x (ppb)	5.58	6.49	19.5	14.0	31.0	12.17	0.22	72.1
SO_4^{2-} (μg/m^3)	3.01	1.60	3.87	1.56	4.65	1.21	0.33	7.3
EC (μg/m^3)	0.37	0.26	0.82	0.45	1.18	0.39	0.05	3.5

Table 4 Subject-Weighted Correlations among Pollutant Variables (raw values)

species	As	benzene	Cl	Diesel	EC	formald	HCl	Hg	Mn	Ni	NO_x	lead	POM	polypro	SO_2	SO_4^{2-}	traffic
arsenic	1.00	0.08	-0.0	0.09	0.10	0.08	0.02	0.03	0.03	0.11	0.12	0.13	0.07	0.05	0.16	0.05	0.08
benzene	0.28	1.00	0.15	0.65	0.71	**0.90**	0.08	0.37	0.26	0.47	**0.71**	0.35	0.64	0.15	0.34	0.09	**0.71**
chlorine	0.14	0.21	1.00	0.04	0.18	0.09	-0.01	0.04	0.23	0.37	0.15	-0.02	-0.09	0.0	0.02	-0.09	0.13
Diesel PM	-0.05	0.36	0.05	1.00	**0.75**	**0.71**	0.08	0.35	0.12	0.33	**0.70**	0.29	0.04	0.09	0.54	0.29	0.65
EC	0.01	0.36	-0.39	0.44	1.00	**0.75**	0.08	0.33	0.17	0.45	**0.96**	0.41	0.43	0.12	0.68	0.33	0.59
formald	0.10	**0.72**	0.03	**0.75**	**0.70**	1.00	0.09	0.40	0.23	0.39	**0.72**	0.43	0.59	0.14	0.44	0.09	0.64
HCl	0.05	0.50	0.14	-0.10	0.23	0.34	1.00	0.05	0.08	0.06	0.08	0.10	0.21	0.01	0.17	0.12	0.03
mercury	0.12	0.57	-0.08	0.64	0.39	0.54	0.13	1.00	0.61	0.21	0.31	0.23	0.31	0.08	0.49	0.19	0.27
Mn	0.18	0.50	0.30	-0.04	-0.04	0.16	0.49	0.43	1.00	0.23	0.14	0.11	0.10	0.03	0.14	0.16	0.15
nickel	0.26	0.67	-0.04	0.23	0.39	0.55	0.03	0.41	0.13	1.00	0.35	0.17	0.35	0.15	0.31	-0.0	0.37
NO_x	0.13	0.44	-0.29	0.26	**0.84**	0.36	0.33	0.24	-0.10	0.51	1.00	0.43	0.45	0.13	0.65	0.20	0.56
lead	0.12	0.07	0.15	0.35	0.47	0.68	0.68	0.48	**0.70**	0.29	0.49	1.00	0.35	0.01	0.44	0.16	0.04
POM	0.20	0.67	0.09	0.24	0.29	0.43	0.13	0.41	0.07	0.52	0.25	0.15	1.00	0.11	0.30	-0.06	0.34
polypro	0.03	0.04	-0.03	0.01	-0.01	0.03	-0.08	-0.01	0.08	0.26	-0.03	-0.07	-0.03	1.00	0.13	0.09	0.15
SO_2	0.05	0.33	-0.39	0.18	**0.75**	0.52	0.48	0.19	0.07	0.32	**0.81**	0.53	-0.07	-0.06	1.00	0.56	0.32
SO_4^{2-}	-0.06	-0.03	-0.52	-0.02	0.39	0.07	0.25	0.08	0.03	-0.01	0.40	0.24	-0.41	-0.19	**0.79**	1.00	0.16
traffic density	0.10	0.68	0.14	0.54	0.36	0.67	0.45	0.60	0.46	0.31	0.27	0.61	0.26	0.05	0.37	0.10	1.00
av'g low	0.08	0.42	0.07	0.38	0.44	0.42	0.08	0.27	0.17	0.27	0.42	0.24	0.30	0.09	0.22	0.26	0.32
av'g high	0.10	0.40	-0.03	0.24	0.32	0.42	0.25	0.32	0.21	0.30	0.31	0.37	0.20	-0.0	0.33	0.11	0.35

Values above the diagonal are for low-traffic density counties; values below the diagonal are for high-density counties.

Table 5 Cumulative mortality risks across all sub-periods (linear exposures)

	all subjects			traffic dens.>7.39x10^6 veh-mi/mi^2			traffic dens.<= 7.39x10^6 veh-mi/mi^2		
	RR	LCI	UCI	RR	LCI	UCI	RR	LCI	UCI
benzene	1.1042	1.0801	1.1289	1.2013	1.1797	1.2234	1.0071	0.9682	1.0491
formaldehyde	1.0866	1.0676	1.1059	1.1248	1.1101	1.1396	1.0137	0.9782	1.0519
diesel PM	1.0797	1.0621	1.0976	1.0510	1.0381	1.0642	1.0737	1.0439	1.1053
oxides of nitrogen	1.0764	1.0612	1.0919	1.1823	1.1685	1.1963	1.0292	1.0115	1.0474
elemental carbon	1.0736	1.0519	1.0958	1.1460	1.1289	1.1633	1.0420	1.0147	1.0707
nickel	1.0553	1.0446	1.0660	1.0964	1.0871	1.1059	1.0229	0.9744	1.0764
polycyclic organics	1.0381	1.0272	1.0491	1.0704	1.0629	1.0779	0.9973	0.9797	1.0155
sulfur dioxide	1.0375	1.0214	1.0539	1.0723	1.0600	1.0846	1.0159	0.9978	1.0347
1985 traffic density	1.0297	1.0221	1.0373	1.0220	1.0139	1.0301	1.0313	1.0154	1.0476
local mercury	1.0257	1.0180	1.0334	1.0288	1.0217	1.0359	1.0008	0.9933	1.0085
1997 traffic density	1.0239	1.0148	1.0331	1.0595	1.0384	1.0810	1.0446	1.0315	1.0579
lead	1.0166	1.0089	1.0243	1.0234	1.0177	1.0291	0.9983	0.9917	1.0051
arsenic	1.0062	0.9977	1.0146	1.0266	1.0220	1.0312	1.0031	0.9996	1.0066
chlorine	1.0048	1.0028	1.0068	1.0195	1.0139	1.0250	1.0039	1.0019	1.0058
hydrochloric acid	1.0030	0.9990	1.0071	1.0114	1.0046	1.0183	1.0004	0.9966	1.0042
polypropylene	1.0028	0.9961	1.0095	1.0052	1.0043	1.0062	1.0005	0.9962	1.0050
manganese	0.9970	0.9896	1.0044	0.9797	0.9738	0.9858	0.9933	0.9858	1.0009
sulfate aerosol	0.9466	0.9195	0.9746	0.9364	0.9142	0.9591	0.9328	0.9046	0.9629

Table 6 Summary of relative mortality risks for all subjects based on 2-pollutant models (1985 traffic density + "other" species) based on linear exposures

	Cumulative (all sub-periods)			1997-2001 sub-period		
other species	traffic	other	total	traffic	other	total
benzene	***1.0123***	***1.0763***	***1.0907***	0.9984	1.1074	1.1056
formaldehyde	1.0042	***1.0800***	***1.0849***	1.0080	1.0662	1.0671
diesel PM	1.0050	***1.0749***	***1.0806***	0.9971	***1.0736***	1.0706
oxides of nitrogen	***1.0102***	***1.0674***	***1.0791***	1.0126	1.0292	1.0422
elemental carbon	***1.0171***	***1.0493***	***1.0682***	1.0147	1.0248	1.0399
nickel	***1.0112***	***1.0477***	***1.0600***	1.0086	1.0326	1.0414
polycyclic organics	***1.0203***	***1.0250***	***1.0463***	1.0149	1.0154	1.0305
sulfur dioxide	***1.0244***	1.0136	***1.0387***	1.0280	0.9628	0.9898
arsenic	***1.0280***	***1.0051***	***1.0334***	1.0197	1.0023	1.0220
chlorine	***1.0281***	***1.0046***	***1.0330***	1.0195	1.0034	***1.0230***
lead	***1.0263***	1.0062	***1.0328***	1.0178	1.0047	1.0226
local mercury	***1.0223***	1.0079	***1.0327***	1.0101	1.0163	1.0266
polypropylene	***1.0275***	1.0021	***1.0298***	1.0192	1.0014	1.0206
hydrochloric acid	***1.0287***	1.0090	***1.0296***	1.0186	1.0063	1.0251
manganese	***1.0335***	***0.9869***	***1.0194***	1.0208	0.9982	1.0190
sulfate aerosol	***1.0305***	***0.9321***	***0.9586***	***1.0220***	0.9351	0.9557

bold italic = $p < 0.05$

Table 7A Comparison of Mortality Risks with Those Based on Measurements[6]

Period	1976-81		1982-88		1989-96	
	measured*	modeled#	measured*	modeled#	measured*	modeled#
NO_2, NO_x	0.049-0.093	0.097 (0.015)	0.029-0.069	0.089 (0.014)	0.014-0.074	0.061 (0.014)
SO_4^{2-}	-0.045 – 0.02	-0.018 (0.029)	-0.13 – 0.05	-0.036 (0.027)	-0.22 - -0.08	-0.10 (0.028)

---

* range of estimated risk coefficients[6] # estimated risk coefficient (standard error)

Table 7B Comparison of 1997-2001 Mortality Risk Coefficients with Those Based on Measurements[7]

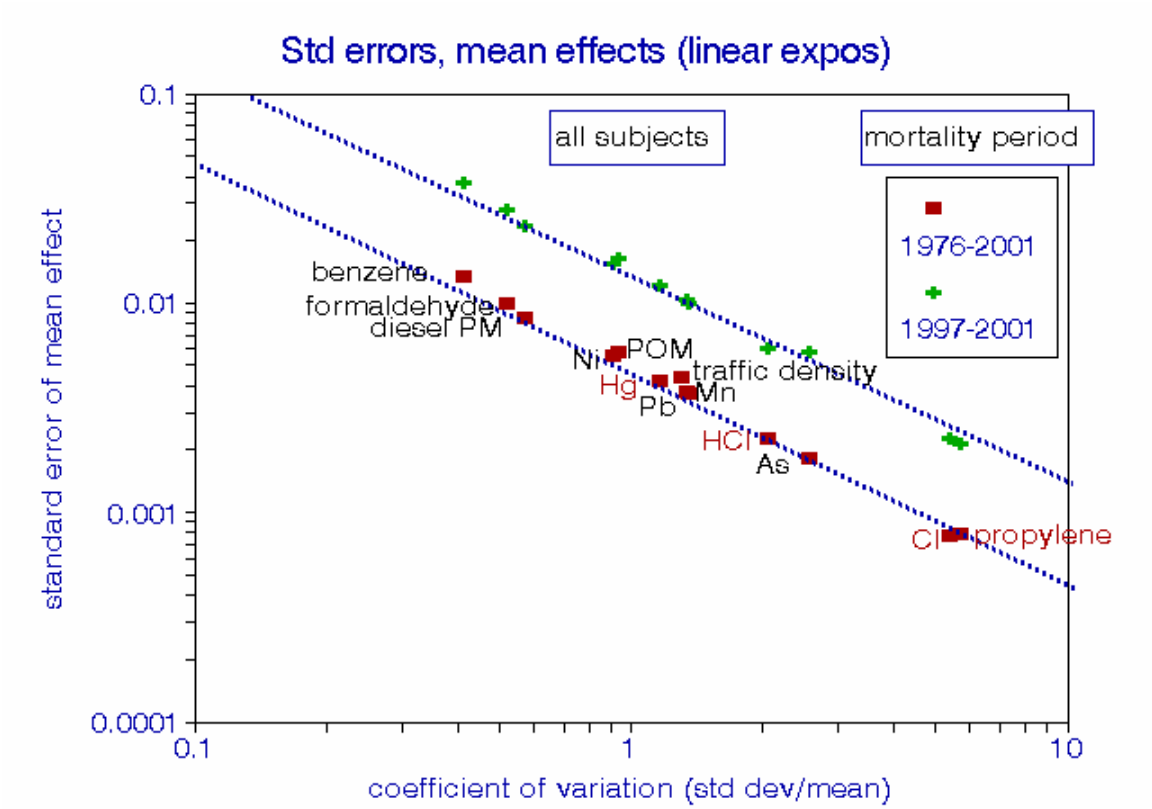
	measured[7]	modeled
NO_2, NO_x	0.086 (0.079)	0.041 (0.022)
EC	0.131 (0.046)	0.045 (0.028)
SO_2	-0.047 (0.043)	-0.012 (0.023)
SO_4^{2-}	0.036 (0.060)	-0.056 (0.042)
Mn	-0.013 (0.014)	0.004 (0.010)
Ni	0.043 (0.020)	0.039 (0.016)
Pb	-0.031 (0.025)	0.011 (0.010)

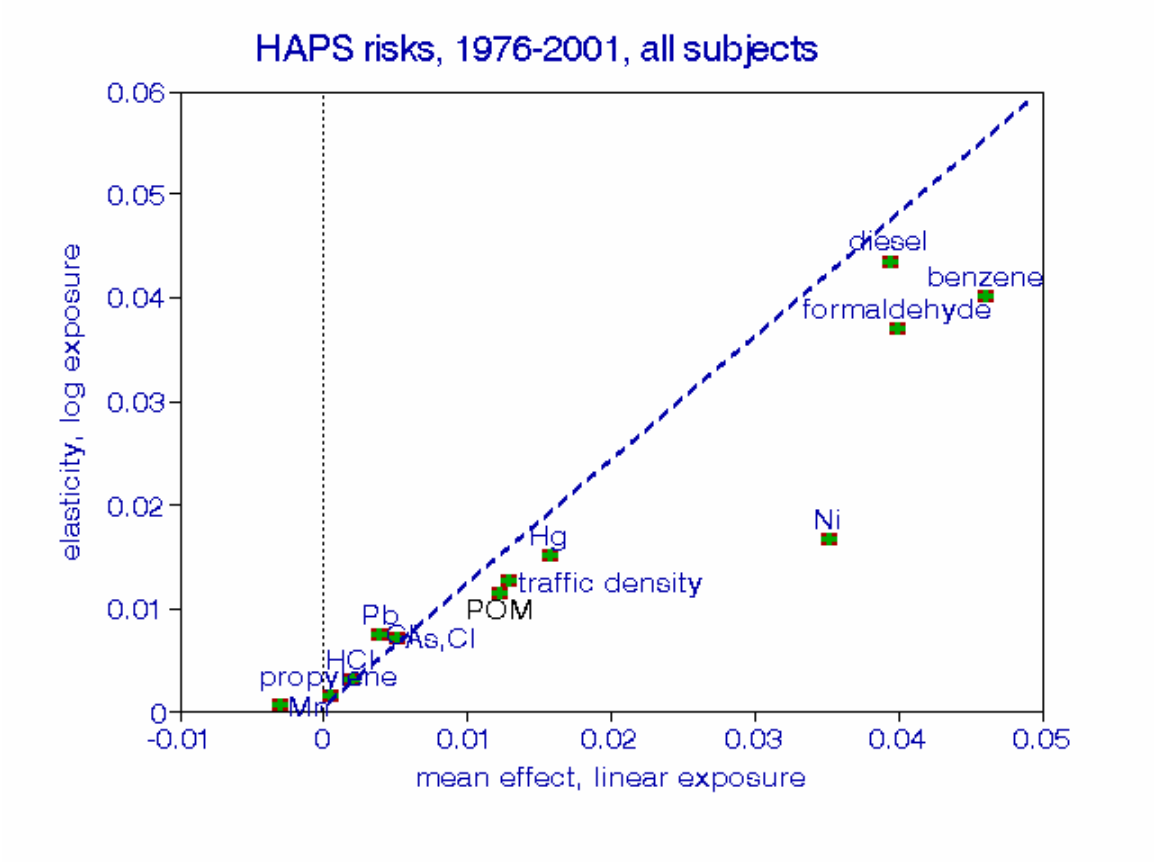
Figure captions

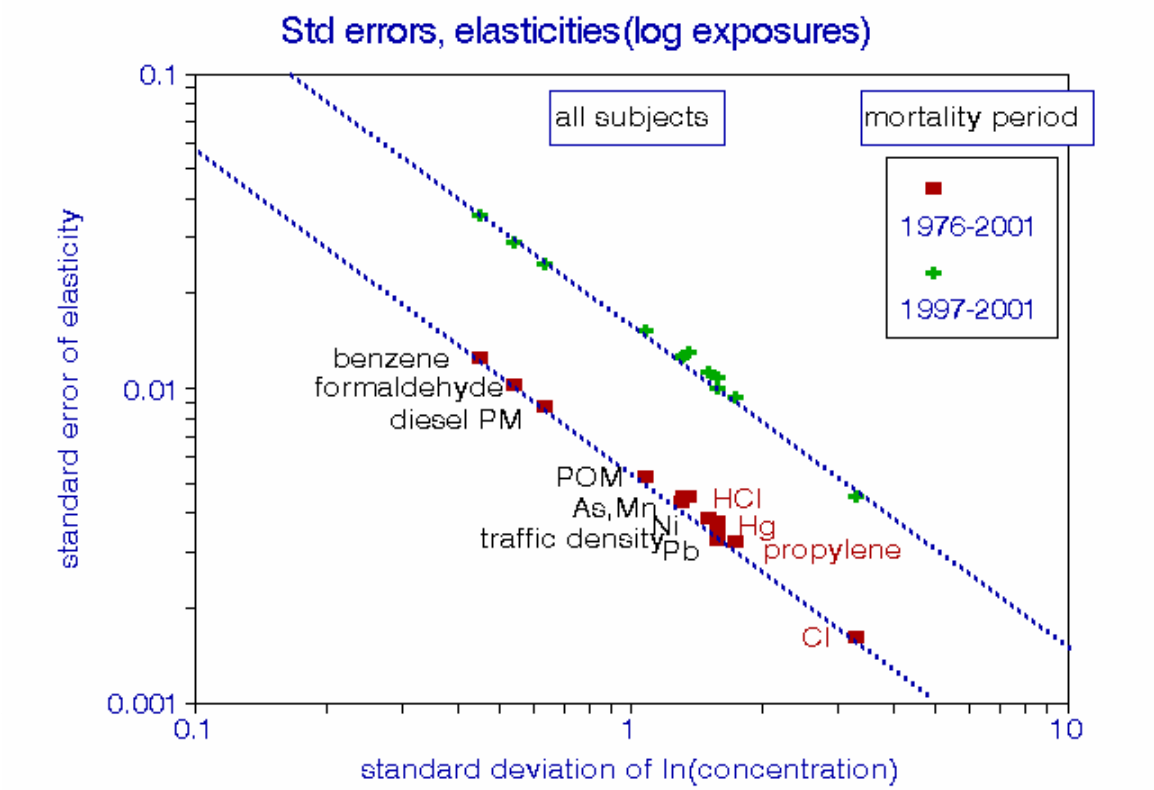
Figure 1. Relationship between risk coefficients (mean effects) and pollutant correlations.
(a) for all subjects, assuming benzene is the "true" pollutant.
(b) for all subjects, assuming NO_x is the "true" pollutant.
(c) for subjects in high traffic-density counties, assuming benzene is the "true" pollutant.
(d) for subjects in high traffic-density counties, assuming NO_x is the "true" pollutant.

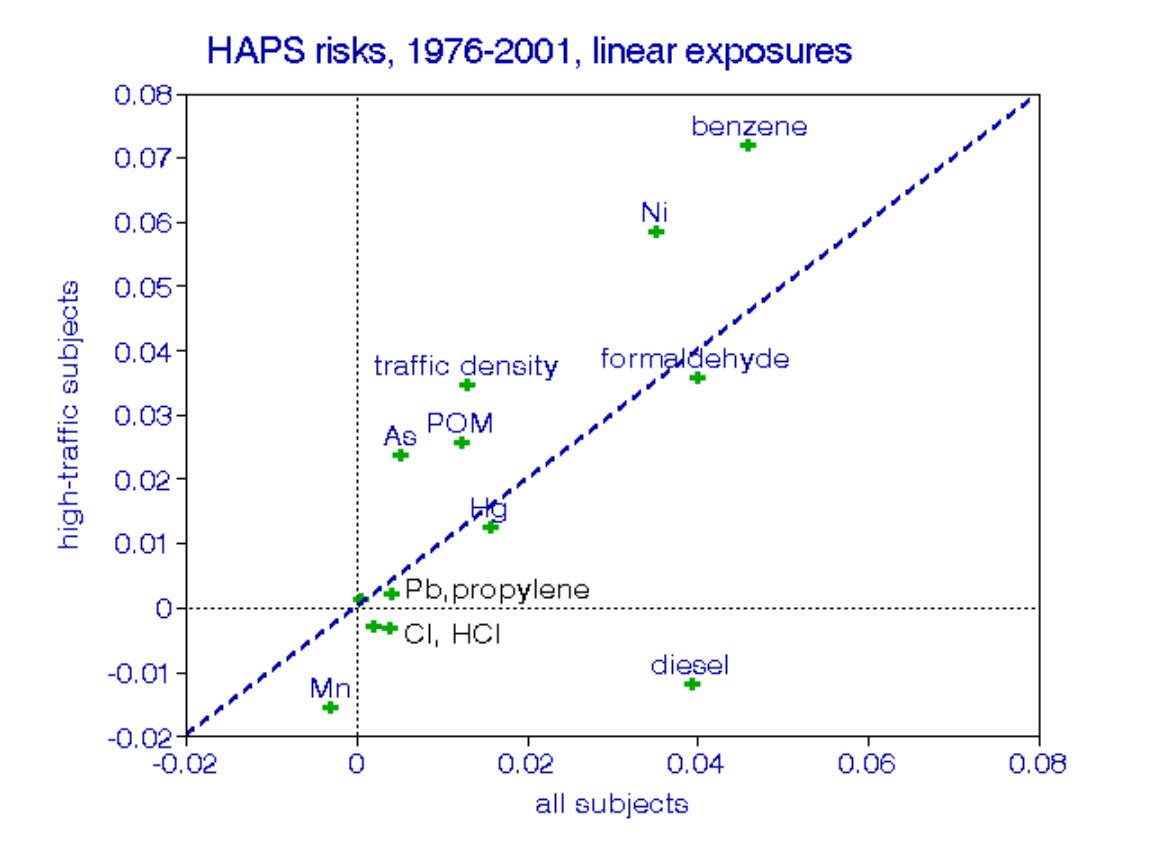
Figure 2. Relationships between the standard errors of mean effects and pollutant coefficients of variation (linear exposure model).

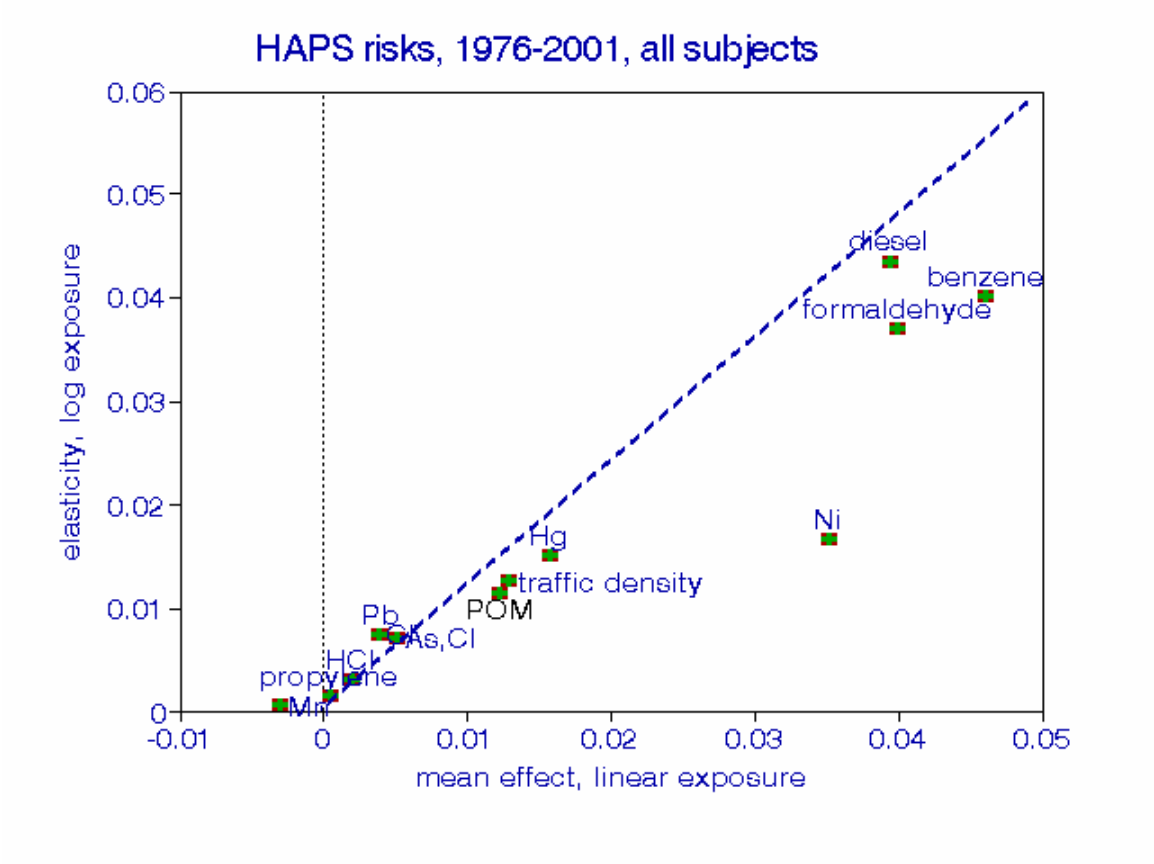
Figure 3. Relative risks from two-pollutant models (linear exposures).

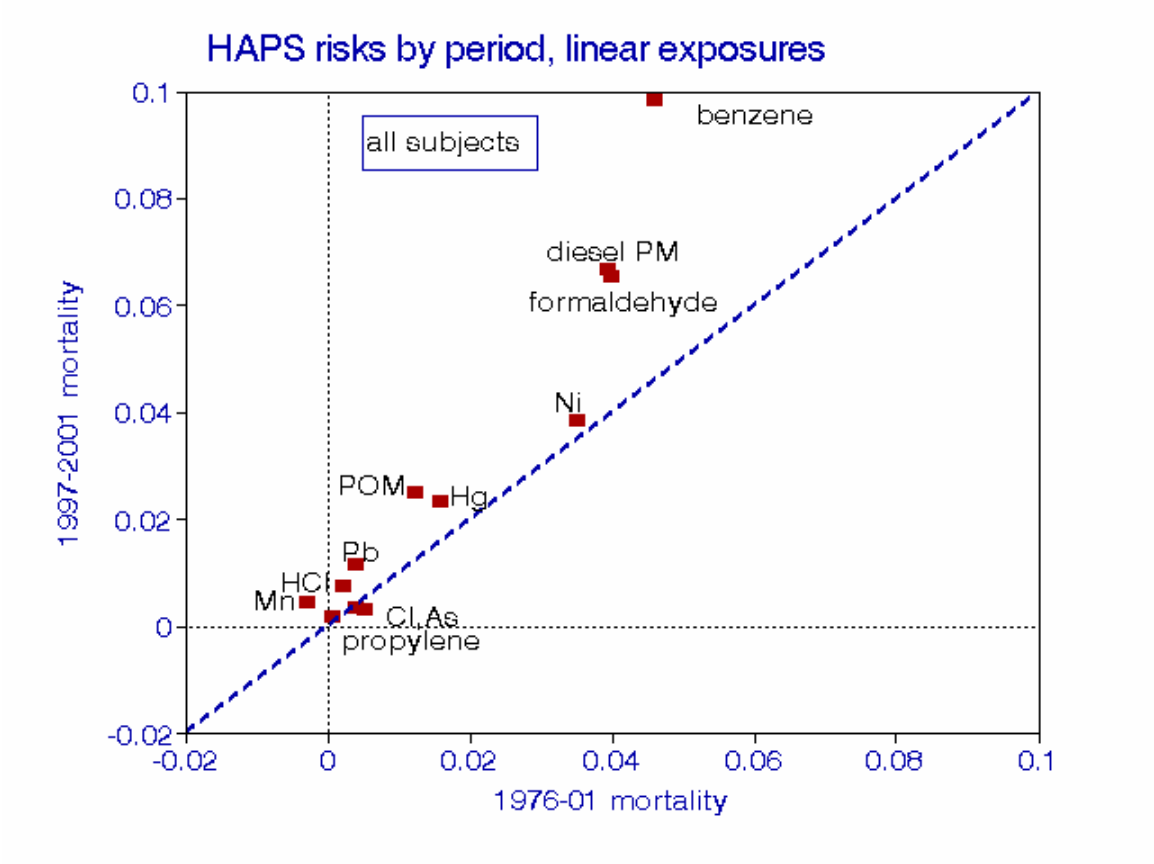



HAPS risks, 1976-2001, all subjects
elasticity, log exposure
mean effect, linear exposure
0.06
0.05
0.04
0.03
0.02
0.01
0
-0.01
0
0.01
0.02
0.03
0.04
0.05
diesel
benzene
formaldehyde
Ni
Hg
traffic density
POM
Pb
As,Cl
HCl
propylene
Mn

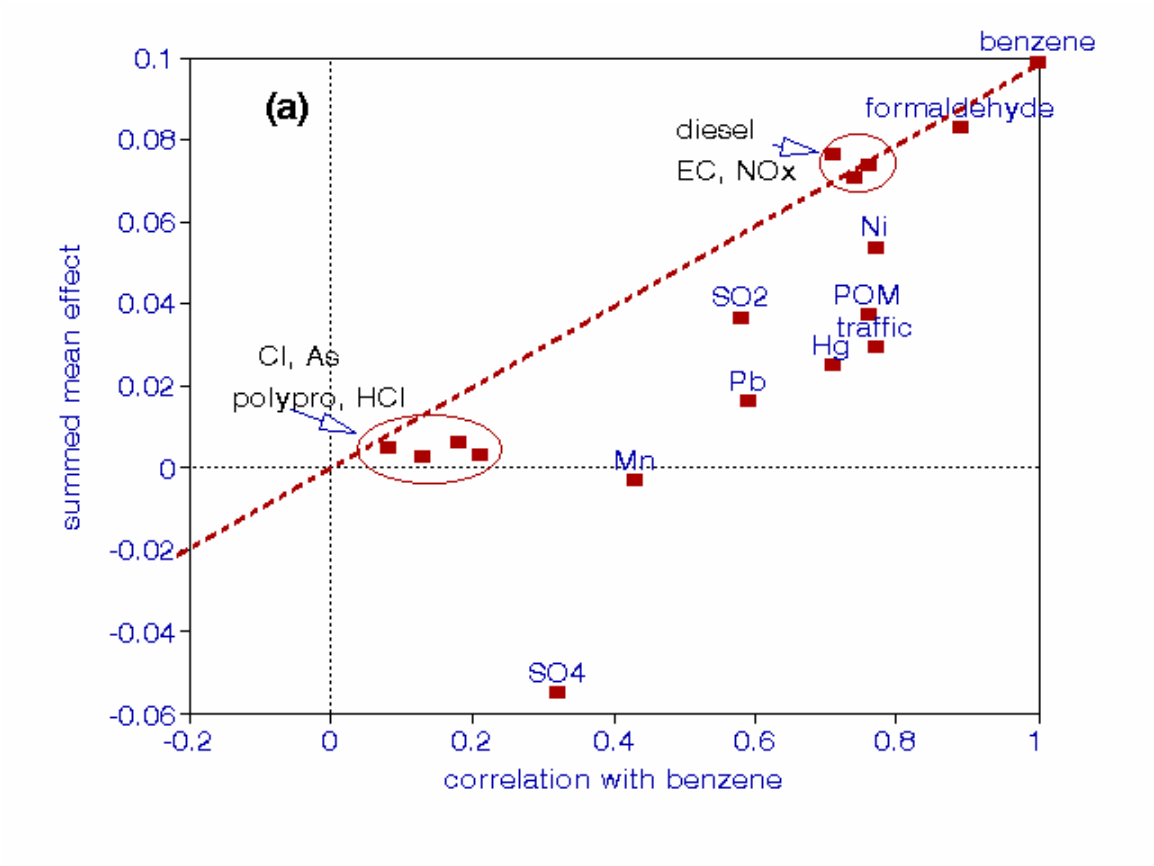

Std errors, elasticities(log exposures)
standard error of elasticity
standard deviation of ln(concentration)
0.1
0.01
0.001
0.1
1
10
all subjects
mortality period
1976-2001
1997-2001
benzene
formaldehyde
diesel PM
POM
As,Mn
Ni
traffic density
Pb
HCl
Hg
propylene
Cl

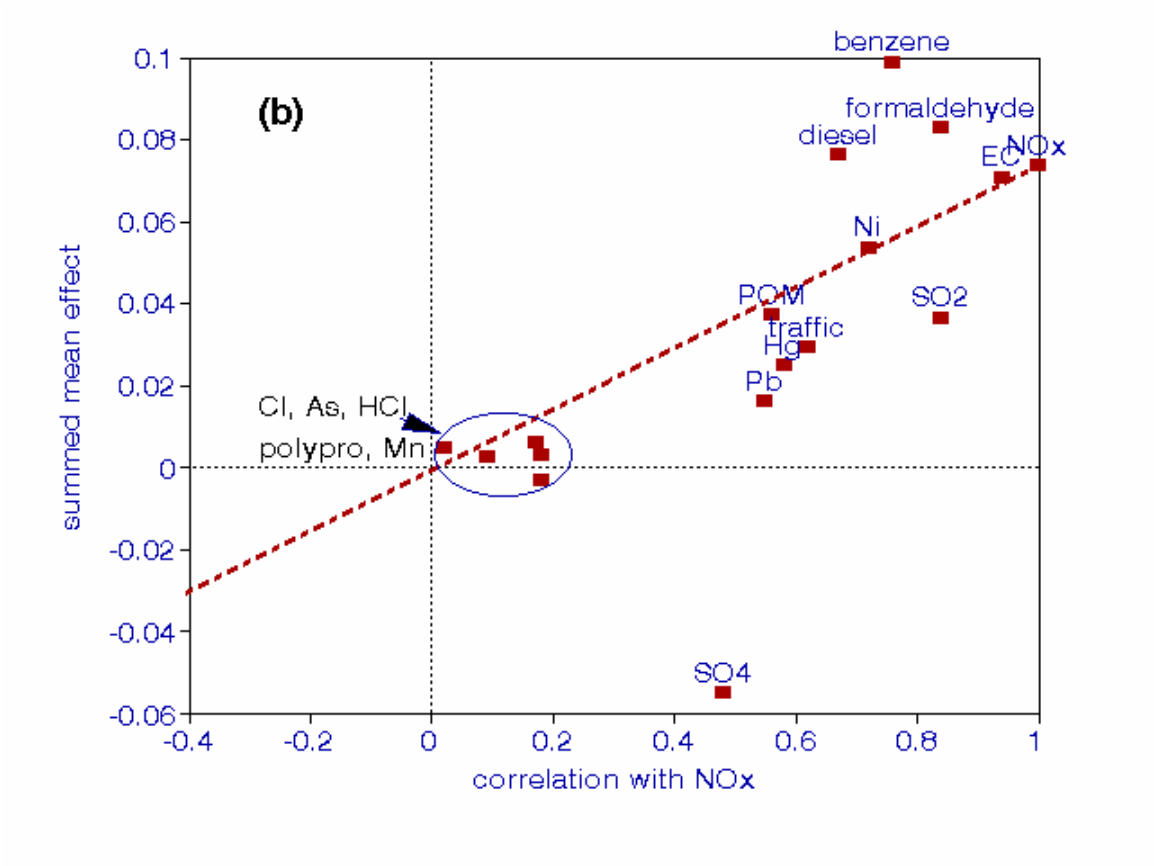

HAPS risks, 1976-2001, linear exposures
high-traffic subjects
all subjects
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
-0.01
-0.02
-0.02
0
0.02
0.04
0.06
0.08
benzene
Ni
traffic density
formaldehyde
As
POM
Hg
Pb, propylene
Cl, HCl
diesel
Mn

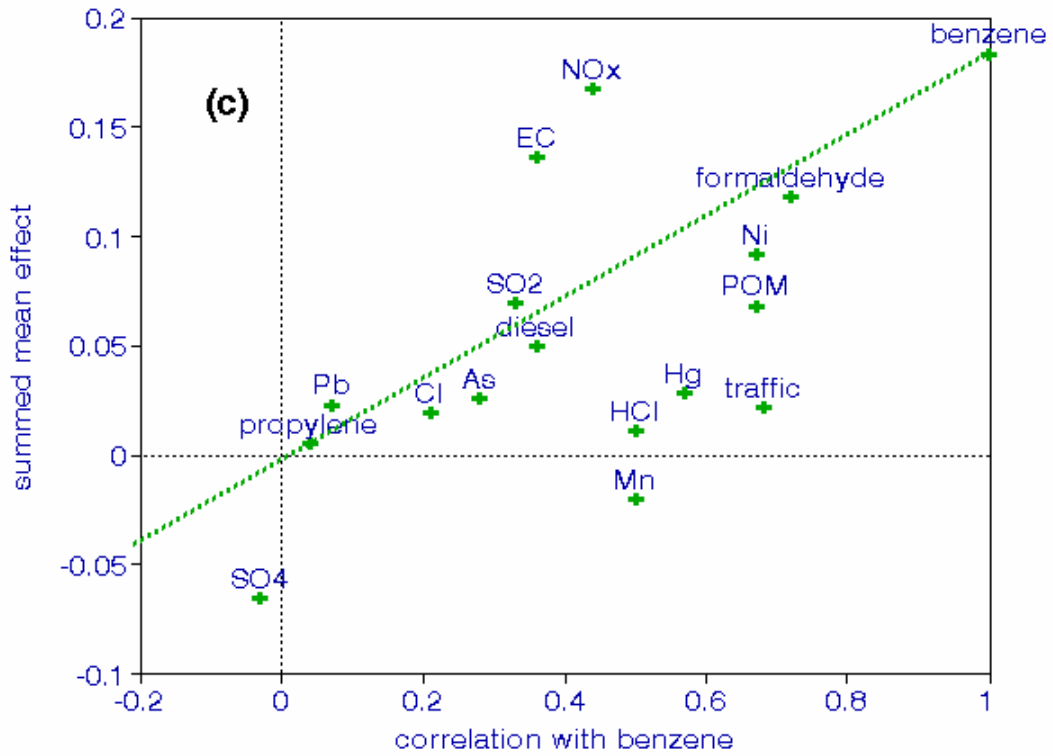

HAPS risks, 1976-2001, all subjects
elasticity, log exposure
mean effect, linear exposure
0.06
0.05
0.04
0.03
0.02
0.01
0
-0.01
0
0.01
0.02
0.03
0.04
0.05
diesel
benzene
formaldehyde
Ni
Hg
traffic density
POM
Pb
As,Cl
HCl
propylene
Mn

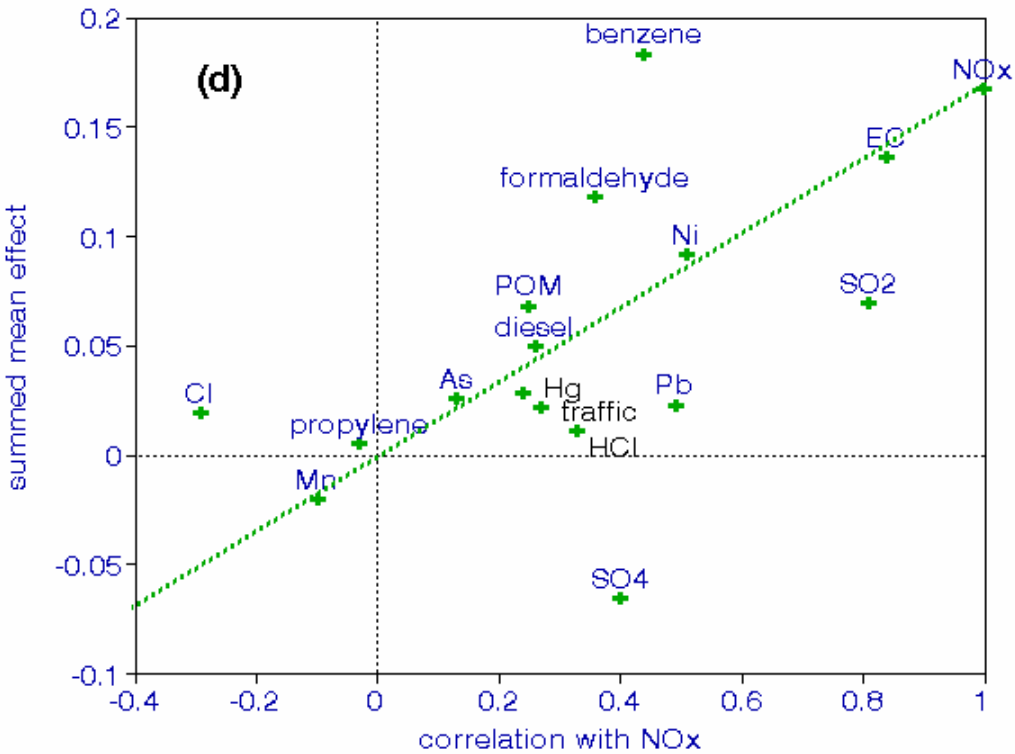

HAPS risks by period, linear exposures
all subjects
benzene
diesel PM
formaldehyde
Ni
POM
Hg
Pb
HCl
Mn
Cl
As
propylene
0.1
0.08
0.06
0.04
0.02
0
-0.02
-0.02
0
0.02
0.04
0.06
0.08
0.1
1997-2001 mortality
1976-01 mortality

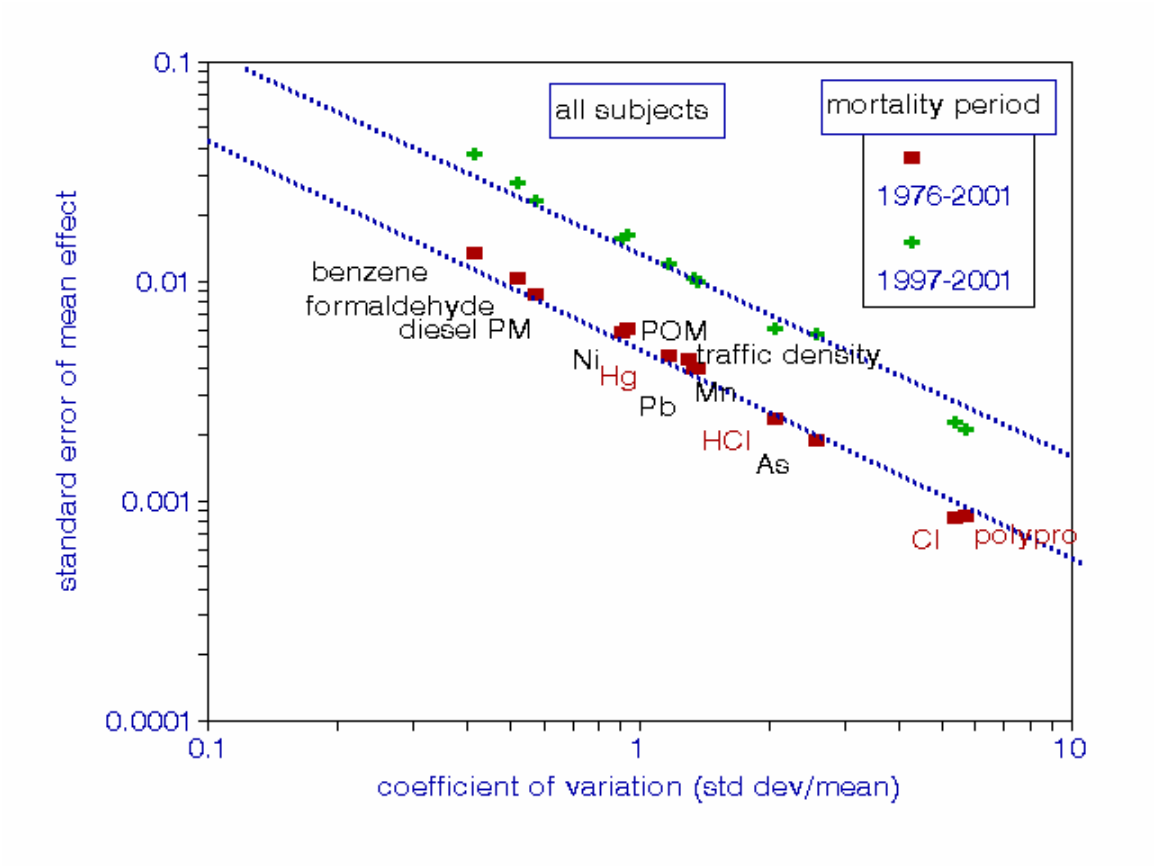
more

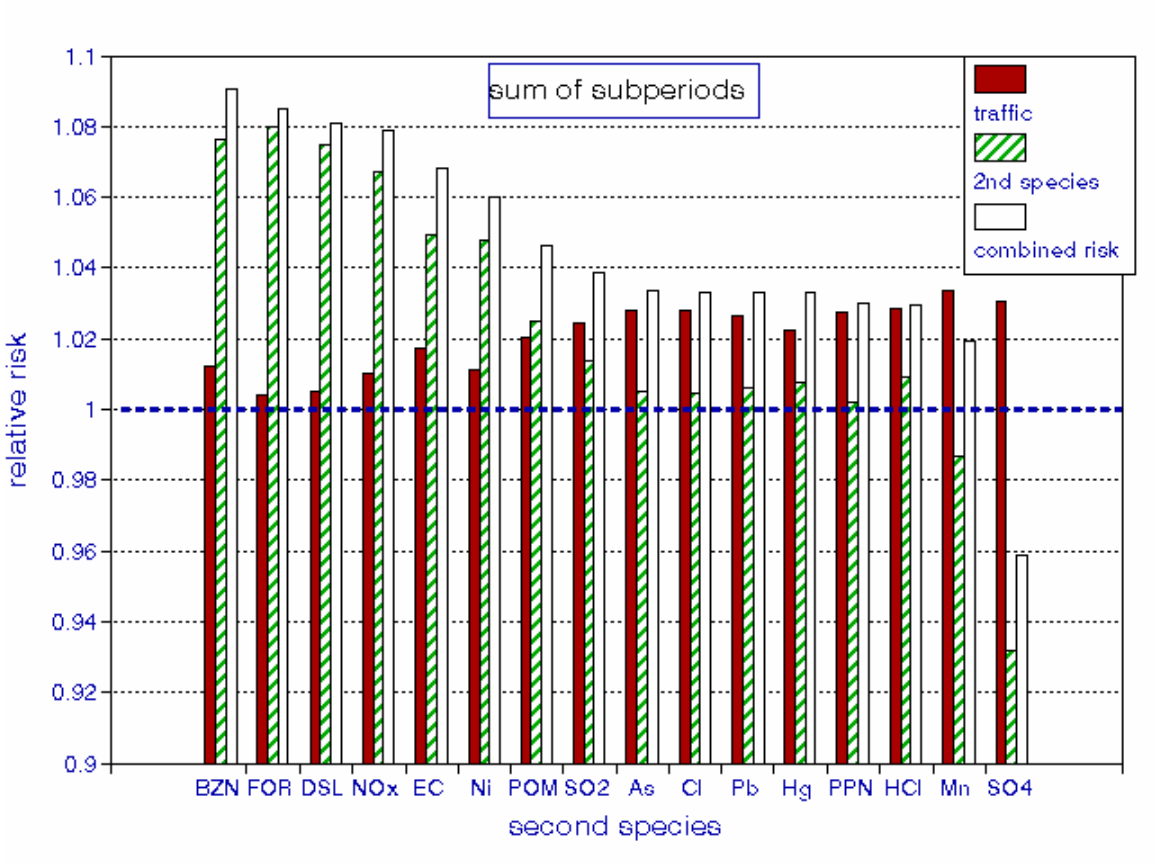

(a)
benzene
formaldehyde
diesel
EC, NOx
Ni
SO2
POM
traffic
Hg
Pb
Cl, As
polypro, HCl
Mn
SO4
summed mean effect
correlation with benzene
0.1
0.08
0.06
0.04
0.02
0
-0.02
-0.04
-0.06
-0.2
0
0.2
0.4
0.6
0.8
1


(b)
benzene
formaldehyde
diesel
EC
NOx
Ni
POM
SO2
traffic
Hg
Pb
Cl, As, HCl
polypro, Mn
SO4
summed mean effect
correlation with NOx
0.1
0.08
0.06
0.04
0.02
0
-0.02
-0.04
-0.06
-0.4
-0.2
0
0.2
0.4
0.6
0.8
1


(c)
benzene
NOx
EC
formaldehyde
Ni
POM
SO2
diesel
Pb
Cl
As
Hg
traffic
HCl
propylene
Mn
SO4
summed mean effect
correlation with benzene
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.2
0
0.2
0.4
0.6
0.8
1


(d)
benzene
NOx
EC
formaldehyde
Ni
POM
SO2
diesel
Cl
As
Hg
Pb
traffic
propylene
HCl
Mn
SO4
summed mean effect
correlation with NOx
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.4
-0.2
0
0.2
0.4
0.6
0.8
1


0.1
0.01
0.001
0.0001
standard error of mean effect
0.1
1
10
coefficient of variation (std dev/mean)
all subjects
mortality period
1976-2001
1997-2001
benzene
formaldehyde
diesel PM
POM
traffic density
Ni
Hg
Pb
Mn
HCl
As
Cl
polypro


sum of subperiods
traffic
2nd species
combined risk
relative risk
1.1
1.08
1.06
1.04
1.02
1
0.98
0.96
0.94
0.92
0.9
BZN
FOR
DSL
NOx
EC
Ni
POM
SO2
As
Cl
Pb
Hg
PPN
HCl
Mn
SO4
second species

Air Pollution and Survival within the Washington University - EPRI Veterans Cohort: Risks Based on Modeled Estimates of Ambient Levels of Hazardous and Criteria Air Pollutants

F.W. Lipfert[1], R.E. Wyzga[2], Jack D. Baty[3], J. Phillip Miller[3]

[1]Consultant, Northport, NY
[2]Technical Executive, Electric Power Research Institute, Palo Alto, CA
[3]Division of Biostatistics, School of Medicine, Washington University, St. Louis, MO

ON-LINE SUPPLEMENT (APPENDICES)

Appendix A. Additional data on the AER and HAPS air quality estimates.

The 10 locations with the highest average concentrations of each AER pollutant are given in Table A-1. The rankings tend to be tightly grouped, especially for SO_4^{2-}, for which 27 counties are included in the ten highest concentration levels. The AER 36x36 km grid square locations did not allow a clear distinction to be made among the five boroughs of New York City, with the exception of the Bronx, which had slightly worse predicted air quality than the other four boroughs. This is consistent with recent detailed air quality surveys in that local area, as discussed below. More than half of these high-pollution locations are in the eastern portion of the nation, where population and traffic densities are also higher. The locations of high SO_2 and SO_4^{2-} levels also reflect the influence of coal-fired power plants, several of which are located in or near Chattooga County, Georgia. New York City, Chicago, and some Louisiana locations appear in all four columns of Table A-1.

Table A-1 Ten Highest Concentration Locations for AER Air Quality Estimates

SO_2	NO_x	SO_4^{2-}	EC
Bronx (NY)	Bronx (NY)	Chattooga County (GA)	Bronx (NY)
Port Huron (MI)	Houston (TX)	Baltimore (MD) area	Boston, Quincy (MA)
east PA, Wilmington,DE	Chicago (IL)	eastern PA, DE	rest of New York City
Chicago (IL)	rest of New York City	Chicago (IL)	Newark (NJ) area
Paterson (NJ)	Newark (NJ) area	Bronx (NY)	Paterson (NJ) area
rest of New York City	St. Charles (LA)	northeast TN, s'west VA	Long Island (NY)
Newark (NJ) area	Paterson (NJ)	Atlanta (GA) area	Houston (TX)
Alton (IL) (St..Louis)	east PA, Wilmington,DE	Gary (IN) area	St. Charles (LA)
Baton Rouge (LA)	Phoenix (AZ)	Washington (DC) area	east PA, Wilmington,DE
Long Island (NY)	Riverside (CA) area	St. Charles (LA)	Chicago (IL)

Tables A-2 and A-3 contain additional correlation matrices. Table A-2 provides correlations of the raw variables for all subjects. Table A-3 has correlations of their logarithms, for all subjects and for subjects residing in counties with high traffic density.

Table A-2 Subject-Weighted Correlations among Pollutant Variables (all subjects)

species	As	benzene	Cl	Diesel	EC	formald	HCl	Hg	Mn	Ni	NO_x	lead	POM	polypro	SO_2	SO_4^{2-}	traffic
arsenic	1.00	0.18	0.01	0.10	0.13	0.14	0.04	0.12	0.10	0.19	0.17	0.16	0.16	0.04	0.16	0.07	0.13
benzene		1.00	0.08	**0.71**	**0.74**	**0.89**	0.21	**0.71**	0.43	**0.77**	**0.76**	0.59	**0.76**	0.13	0.58	0.32	**0.77**
chlorine			1.00	0.01	0.02	0.02	-0.001	-0.01	0.20	0.15	0.02	0.02	-0.03	0.004	-0.06	-0.20	0.02
diesel PM				1.00	**0.75**	**0.85**	0.10	**0.74**	0.19	0.57	0.67	0.46	0.53	0.10	0.55	0.36	**0.72**
elemental carbon					1.00	**0.85**	0.17	0.64	0.21	0.67	**0.94**	0.54	0.57	0.10	**0.82**	0.52	0.65
formaldehyde						1.00	0.19	**0.75**	0.30	**0.73**	**0.84**	0.62	0.66	0.12	0.68	0.38	**0.80**
hydrochoric acid							1.00	0.12	0.19	0.12	0.18	0.25	0.18	-0.004	0.26	0.18	0.20
mercury								1.00	0.52	0.62	0.58	0.49	0.60	0.07	0.49	0.33	**0.74**
manganese									1.00	0.29	0.18	0.42	0.19	0.09	0.21	0.20	0.38
nickel										1.00	**0.72**	0.40	0.65	0.25	0.56	0.28	0.61
oxides on nitrtogen											1.00	0.55	0.56	0.09	**0.84**	0.48	0.62
lead												1.00	0.36	0.01	0.57	0.31	0.52
polycyclic organic materials													1.00	0.36	0.33	0.06	0.54
polypropylene														1.00	0.05	-0.02	0.13
sulfur dioxide															1.00	**0.71**	0.58
sulfate aerosol																1.00	0.35
traffic density																	1.00

Table A-3 Subject-Weighted Correlations among the Logarithms of Pollutant Variables)

species	As	Bzn	Cl	Diesel	EC	Form	HCl	Hg	Mn	Ni	NO_x	Pb	POM	Ppn	SO_2	SO_4^{2-}	traffic
As	1.00	**0.73**	0.56	0.64	0.66	**0.71**	0.62	0.69	0.69	**0.75**	**0.70**	**0.73**	**0.72**	0.60	0.54	0.30	0.63
Bzn	0.68	1.00	0.56	**0.80**	**0.81**	**0.94**	0.68	**0.88**	0.68	**0.85**	**0.84**	**0.82**	**0.87**	0.69	0.55	0.25	**0.86**
Cl	0.53	0.56	1.00	0.50	0.50	0.53	0.52	0.50	0.54	0.57	0.51	0.49	0.48	0.50	0.41	0.29	0.51
Diesel	0.04	0.34	0.02	1.00	**0.84**	**0.86**	0.63	**0.85**	0.59	**0.78**	**0.83**	**0.74**	**0.74**	0.62	0.63	0.41	**0.81**
EC	0.28	0.38	-0.20	0.33	1.00	**0.87**	0.66	**0.82**	0.56	**0.77**	**0.95**	**0.77**	**0.71**	0.61	**0.78**	0.49	**0.81**
Form	0.45	**0.75**	0.28	0.68	0.68	1.00	0.67	**0.87**	0.63	**0.81**	**0.86**	**0.82**	**0.82**	0.68	0.59	0.32	**0.86**
HCl	0.22	0.48	0.10	-0.10	0.34	0.40	1.00	**0.70**	0.66	0.68	0.68	**0.75**	0.64	0.49	0.65	0.41	0.64
Hg	0.54	0.56	0.06	0.42	0.46	0.53	0.17	1.00	**0.73**	**0.86**	**0.83**	**0.82**	**0.86**	**0.70**	0.63	0.35	**0.86**
Mn	0.40	0.40	0.30	0.02	0.02	0.14	0.25	0.64	1.00	**0.73**	0.58	**0.70**	0.64	0.58	0.46	0.26	0.61
Ni	**0.72**	0.69	0.53	0.24	0.43	0.61	0.12	0.50	0.24	1.00	**0.82**	**0.79**	**0.84**	**0.71**	0.60	0.26	**0.80**
NO_x	0.48	0.50	0.04	0.21	**0.88**	**0.70**	0.45	0.44	0.0	0.55	1.00	**0.81**	**0.76**	0.66	**0.75**	0.40	**0.81**
Pb	0.46	0.68	0.23	0.30	0.61	**0.73**	0.64	0.57	0.47	0.45	0.69	1.00	**0.79**	0.60	0.60	0.29	**0.71**
POM	0.65	**0.75**	0.47	0.31	0.39	0.59	0.10	0.66	0.25	0.69	0.44	0.38	1.00	**0.70**	0.47	0.15	**0.74**
Ppn	0.37	0.30	0.39	0.22	0.20	0.39	-0.21	0.28	0.16	0.46	0.24	0.14	0.40	1.00	0.37	0.13	0.66
SO_2	0.28	0.24	-0.28	-0.04	0.60	0.25	0.39	0.21	0.03	0.30	0.63	0.35	0.0	-0.22	1.00	**0.79**	0.63
SO_4^{2-}	0.02	-0.06	-0.44	-0.15	0.39	-0.09	0.20	0.0	-0.02	0.0	0.30	0.08	-0.32	-0.42	**0.90**	1.00	0.42
traffic density	0.41	**0.72**	0.19	0.39	0.44	**0.70**	0.48	0.49	0.34	0.39	0.41	0.63	0.39	0.25	0.32	0.09	1.00

Values above the diagonal are for all subjects; values below the diagonal are for high-density counties.

Appendix B. Additional Mortality Risk Estimates

This Appendix includes risk estimates based on the logarithms of the pollutant variables: Table B-1 compares with Table 5 in the main text, and Table B-2 compares with Table 6. Table B-3 contains the (non-logarithmic) risk estimates by mortality sub-period that were used to construct Table 5 in the main text. Downward trends are seen for elemental carbon, formaldehyde, nitrogen oxides, nickel, sulfur dioxide, and sulfates.

Table B-1 Cumulative mortality risks across all subperiods (logarithmic exposures)

	all subjects			traffic dens.>7.39x10^6 veh-mi/mi^2			traffic dens.< =7.39x10^6 veh-mi/mi^2		
	RR	LCI	UCI	RR	LCI	UCI	RR	LCI	UCI
benzene	1.0887	1.0646	1.1133	1.2583	1.2320	1.2852	1.0122	0.9754	1.0519
diesel PM	1.0786	1.0615	1.0961	1.1022	1.0793	1.1256	1.0506	1.0244	1.0781
formaldehyde	1.0769	1.0567	1.0973	1.1687	1.1485	1.1892	1.0189	0.9842	1.0562
elemental carbon	1.0570	1.0380	1.0763	1.1204	1.1006	1.1405	1.0377	1.0083	1.0689
oxides of nitrogen	1.0480	1.0356	1.0606	1.1400	1.1256	1.1546	1.0216	1.0037	1.0403
polycyclic organics	1.0308	1.0204	1.0413	1.1043	1.0924	1.1163	1.0022	0.9884	1.0164
nickel	1.0296	1.0220	1.0374	1.1104	1.0976	1.1233	1.0143	1.0043	1.0245
1985 traffic density	1.0286	1.0221	1.0352	1.0577	1.0471	1.0685	1.0193	1.0084	1.0304
1997 traffic density	1.0260	1.0194	1.0327	1.1011	1.0799	1.1228	1.0581	1.0464	1.0700
local mercury	1.0257	1.0180	1.0334	1.0380	1.0272	1.0489	1.0135	1.0026	1.0247
lead	1.0195	1.0131	1.0260	1.0493	1.0425	1.0561	1.0020	0.9937	1.0104
sulfur dioxide	1.0163	1.0032	1.0294	1.0342	1.0235	1.0450	1.0111	0.9939	1.0289
arsenic	1.0161	1.0073	1.0250	1.0807	1.0703	1.0913	0.9982	0.9874	1.0092
chlorine	1.0145	1.0113	1.0177	1.0174	1.0142	1.0205	1.0031	0.9996	1.0067
polypropylene	1.0129	1.0061	1.0198	1.0469	1.0413	1.0526	0.9791	0.9702	0.9882
hydrochloric acid	1.0111	1.0022	1.0200	1.0249	1.0159	1.0340	0.9928	0.9824	1.0034
manganese	1.0045	0.9960	1.0132	0.9761	0.9666	0.9858	0.9929	0.9827	1.0033
sulfate aerosol	0.9823	0.9628	1.0022	0.9802	0.9632	0.9974	0.9745	0.9517	0.9983

Table B-2 Summary of cumulative mortality risks across all subperiods for all subjects based on 2-pollutant models (1985 traffic density + "other" species), based on logarithmic exposures

other species	traffic	other	total
benzene	***1.0298***	0.9975	1.0271
formaldehyde	***1.0259***	1.0116	1.0381
diesel PM	***1.0133***	***1.0513***	***1.0660***
oxides of nitrogen	***1.0236***	1.0143	***1.0386***
elemental carbon	***1.0342***	0.9824	1.0154
nickel	***1.0227***	1.0098	***1.0329***
polycyclic organics	***1.0300***	0.9984	***1.0283***
sulfur dioxide	***1.0355***	***0.9791***	1.0131
arsenic	***1.0323***	0.9927	***1.0245***
chlorine	***1.0214***	***1.0104***	***1.0322***
lead	***1.0278***	1.0020	***1.0300***
local mercury	***1.0324***	0.9954	***1.0275***
polypropylene	***1.0345***	0.9916	***1.0255***
hydrochloric acid	***1.0364***	***0.9836***	***1.0188***
manganese	***1.0391***	0.9773	1.1036
sulfate aerosol	***1.0336***	***0.9567***	0.9874

bold italic = $p < 0.05$

Table B-3 Trends in mortality risks

pollutant	period	all subjects			subjects in high-density cos			pollutant	period	all subjects			subjects in high-density cos		
		RR	LCI	UCI	RR	LCI	UCI			RR	LCI	UCI	RR	LCI	UCI
arsenic	1976-81	1.0057	1.0000	1.0116	1.0191	0.9947	1.0441	manganese	1976-81	0.9942	0.9800	1.0086	0.9645	0.9341	0.9959
arsenic	1982-88	1.0091	1.0033	1.0148	1.0354	1.0128	1.0585	manganese	1982-88	1.0007	0.9882	1.0135	0.9777	0.9500	1.0062
arsenic	1989-96	1.0048	0.9971	1.0126	1.0258	1.0026	1.0496	manganese	1989-96	0.9923	0.9789	1.0059	0.9853	0.9569	1.0145
arsenic	1997-01	1.0032	0.9920	1.0146	1.0258	0.9918	1.0610	manganese	1997-01	1.0045	0.9844	1.0249	1.0065	0.9636	1.0512
benzene	1976-81	1.1067	1.0523	1.1640	1.1500	1.0304	1.2835	nitrogen oxides	1976-81	1.1014	1.0695	1.1343	1.2418	1.1518	1.3389
benzene	1982-88	1.1072	1.0568	1.1601	1.2135	1.0973	1.3421	nitrogen oxides	1982-88	1.0933	1.0641	1.1233	1.2654	1.1815	1.3553
benzene	1989-96	1.1191	1.0663	1.1746	1.4268	1.2864	1.5826	nitrogen oxides	1989-96	1.0626	1.0332	1.0928	1.1675	1.0876	1.2534
benzene	1997-01	1.1033	1.0255	1.1870	1.0506	0.8954	1.2325	nitrogen oxides	1997-01	1.0424	0.9992	1.0875	1.0673	0.9597	1.1869
chlorine	1976-81	1.0051	1.0024	1.0078	1.0074	0.9782	1.0375	nickel	1976-81	1.0648	1.0424	1.0877	1.0740	1.0232	1.1273
chlorine	1982-88	1.0058	1.0032	1.0083	1.0103	0.9840	1.0373	nickel	1982-88	1.0581	1.0373	1.0794	1.1136	1.0657	1.1636
chorinel	1989-96	1.0040	1.0011	1.0069	1.0341	1.0064	1.0626	nickel	1989-96	1.0560	1.0344	1.0781	1.1373	1.0863	1.1907
chlorine	1997-01	1.0035	0.9991	1.0080	1.0360	0.9941	1.0797	nickel	1997-01	1.0393	1.0068	1.0729	1.0534	0.9781	1.1346
diesel PM	1976-81	1.0832	1.0492	1.1183	1.0158	0.9499	1.0863	polycyclic organics	1976-81	1.0340	1.0121	1.0563	1.0517	1.0116	1.0933
diesel PM	1982-88	1.0830	1.0517	1.1152	1.0265	0.9655	1.0913	polycyclic organics	1982-88	1.0319	1.0119	1.0523	1.0601	1.0229	1.0986
diesel PM	1989-96	1.0891	1.0569	1.1222	1.1302	1.0660	1.1982	polycyclic organics	1989-96	1.0569	1.0361	1.0782	1.1320	1.0925	1.1728
diesel PM	1997-01	1.0691	1.0216	1.1189	1.0308	0.9380	1.1327	polycyclic organics	1997-01	1.0253	0.9947	1.0568	1.0245	0.9701	1.0819
elemental carbon	1976-81	1.1076	1.0657	1.1512	1.1948	1.0905	1.3091	lead	1976-81	1.0149	1.0006	1.0293	1.0182	0.9881	1.0492
elemental carbon	1982-88	1.0756	1.0379	1.1147	1.1644	1.0715	1.2653	lead	1982-88	1.0236	1.0107	1.0367	1.0332	1.0053	1.0618
elemental carbon	1989-96	1.0634	1.0250	1.1033	1.1715	1.0760	1.2755	lead	1989-96	1.0135	1.0004	1.0268	1.0260	0.9975	1.0552
elemental carbon	1997-01	1.0464	0.9904	1.1057	1.0479	0.9208	1.1926	lead	1997-01	1.0116	0.9921	1.0314	1.0075	0.9655	1.0514
formaldehyde	1976-81	1.1015	1.0608	1.1438	1.1086	1.0284	1.1950	polypropylene	1976-81	1.0016	0.9984	1.0049	1.0021	0.9969	1.0074
formaldehyde	1982-88	1.0885	1.0513	1.1270	1.1185	1.0439	1.1985	polypropylene	1982-88	1.0031	1.0004	1.0059	1.0059	1.0014	1.0104
formaldehyde	1989-96	1.0930	1.0533	1.1342	1.2307	1.1473	1.3202	polypropylene	1989-96	1.0040	1.0013	1.0067	1.0080	1.0036	1.0123
formaldehyde	1997-01	1.0678	1.0111	1.1277	1.0282	0.9208	1.1481	polypropylene	1997-01	1.0019	0.9977	1.0060	1.0037	0.9970	1.0105
hydrochloric acid	1976-81	0.9995	0.9909	1.0081	1.0081	0.9728	1.0447	sulfur dioxide	1976-81	1.0634	1.0314	1.0964	1.1054	1.0355	1.1799
hydrochloric acid	1982-88	1.0019	0.9945	1.0095	1.0133	0.9807	1.0471	sulfur dioxide	1982-88	1.0495	1.0201	1.0797	1.1205	1.0551	1.1900
hydrochloric acid	1989-96	1.0055	0.9977	1.0133	1.0196	0.9860	1.0543	sulfur dioxide	1989-96	1.0271	0.9975	1.0575	1.0507	0.9874	1.1181
hydrochloric acid	1997-01	1.0077	0.9958	1.0197	0.9962	0.9470	1.0478	sulfur dioxide	1997-01	0.9881	0.9454	1.0326	0.9748	0.8885	1.0695
local mercury	1976-81	1.0178	1.0017	1.0341	1.0037	0.9677	1.0410	sulfate aerosol	1976-81	0.9818	0.9275	1.0392	0.9958	0.8793	1.1278
local mercury	1982-88	1.0282	1.0137	1.0429	1.0195	0.9863	1.0539	sulfate aerosol	1982-88	0.9650	0.9155	1.0173	1.0286	0.9183	1.1522
local mercury	1989-96	1.0323	1.0170	1.0478	1.0666	1.0312	1.1032	sulfate aerosol	1989-96	0.9039	0.8563	0.9542	0.8487	0.7561	0.9528
local mercury	1997-01	1.0238	0.9999	1.0481	1.0250	0.9711	1.0819	sulfate aerosol	1997-01	0.9454	0.8715	1.0255	0.8593	0.7246	1.0191
’85 traffic density	1976-81	1.0263	1.0099	1.0429	0.9959	0.9540	1.0396								
’85 traffic density	1982-88	1.0238	1.0090	1.0388	0.9860	0.9489	1.0245								

’85 traffic density	1989-96	1.0452	1.0299	1.0606	1.0848	1.0451	1.1260
’85 traffic density	1997-01	1.0200	0.9982	1.0422	1.0350	0.9801	1.0930

Appendix C. Comparisons with Previous Long-Term Mortality Studies.

No other U.S. cohort study has examined mortality risks associated with traffic exposures on a national basis. However, there are relevant studies in the literature:

Finkelstein et al.[1] found a relative risk of 1.18 for all-cause mortality associated with living near major roads in Hamilton, Ontario.

Tonne et al.[2] reported a 5% (3-6%) increase in heart attack risk associated with living near major roads in Worcester, MA, after adjusting for $PM_{2.5}$ emissions sources.

Hoffmann et al.[3] found an odds ratio of 1.85 (1.21-2.34) for the prevalence of coronary heart disease associated with living near major roads in Germany.

Gehring et al.[4] reported a relative risk of 1.29 (0.93-1.78) for all-cause mortality associated with living near major roads in the Ruhr area of Germany and a relative risk of 1.47 (1.05-2.04) associated with the mean concentration of NO_2.

Rosenlund et al.[5] used emissions data and dispersion modeling to estimate NO_2 concentrations at home addresses due to traffic, the median levels of which were associated with relative risks for fatal heart attacks of 1.22 (0.98-1.50) for all cases and 1.44 (1.02-2.04) for out-of-hospital deaths.

Elliott et al.[6] report an ecological study of mortality in Great Britain for four 4-y periods from 1982-98, based on routine monitoring of black smoke (EC) and SO_2 in electoral wards. Using the methods of the present study to estimate risks at mean concentration levels for the total follow-up period, we find relative risks of 1.13 for smoke and 1.02 for SO_2.

Nafstad et al.[7] estimated NO_x and SO_2 levels for the home addresses of 16,209 male residents of Oslo, Norway. Their relative risks for all-cause mortality were 1.13 (1.10-1.19) for NO_x and 0.97 (0.94-1.02) for SO_2, based on estimated mean concentration levels.

Naess et al.[8] used dispersion modeling to estimate PM and NO_2 levels for all 470 local districts of Oslo, Norway. Based on the fragmentary information they reported for NO_2, the all-cause mortality risk for the elderly is 1.29 and is essentially linear. For the 51-70 age group, there is a definite threshold at about 20 ppb with a steeper slope thereafter.

Hoek et al.[9] reported on a small study in the Netherlands that associated all-cause mortality with living near a major road (RR=1.41 [0.94-2.12]) and with mean levels of black smoke (RR=1.52 [0.92-2.49]) and NO_2 (RR=1.31 [0.80-1.36]).

Beelen et al.[10] studied associations between 1987-1996 mortality in a Dutch cohort of about 120,000 subjects, in relation to traffic variables and selected criteria air pollutants. They found substantial differences according to the degree of confounder adjustment; detailed data were available for only about 12% of the full cohort, for which no excess all-cause mortality risks were reported. After adjustment for age, sex, smoking, and area-wide socioeconomic status, relative risks based on mean-minimum concentrations were 1.059 (1.0-1.117) for NO_2, 1.039 (1-1.085) for black smoke (~EC), 1.031 (0.983-1.082) for $PM_{2.5}$, and 0.986 (0.951-1.023) for SO_2. Traffic intensity on the nearest road was also a significant predictor, for the full cohort only (RR=1.03 [1.0-1.08]). In a separate publication, no significant associations were found with lung cancer.

The widely cited U.S. cohort studies by Dockery et al.[11] and Pope et al.[12,13] do not consider traffic impacts. However, the Six Cities Study[11] is dominated by the high pollution levels in Steubenville, OH, where elevated levels of benzene may have also been present from coke oven operations but were not considered in the analysis. Table

C-1 compares ACS and Six Cities findings with those of the present study, on the basis of mean concentration levels of relevant pollutants. Estimated risks for SO_2 agree among the four studies, but there are significant differences for SO_4^{2-}.that might relate to the use of contextual variables in the present study and not in the others. When SO_2 and SO_4^{2-} were regressed jointly in the ACS reanalysis,[14] the SO_4^{2-} risk diminished markedly and lost significance; thus, SO_2 is statistically a better mortality predictor than SO_4^{2-}. Comparing Tables 6 and 7 of Lipfert et al.[15] shows that sulfate mortality risks are sensitive to the use of contextual variables in the proportional hazards modeling. For NO_x, our results agree with the Six Cities study, but not with the ACS estimates, which may have been limited by the availability of ambient monitoring data. However, pollutant exposures in the ACS study are based on multi-county metropolitan statistical areas and thus that study may not be able to detect the local effects of traffic and NOx. Table C-1 also shows that the present study has much tighter confidence intervals than the other studies.

Lipfert et al.[16] used modeled estimates of SO_2, SO_4^{2-} and NO_x to predict excess all-cause mortality in 916 U.S. cities for 1980 in an ecological analysis that included state-level estimates of smoking prevalence. The dispersion model used for these estimates was much less complex than the one used in the present analysis, but the relative risk estimates obtained (1.05 – 1.08) are similar. Estimates were also reported for measured Mn and Pb;[16] risks associated with measured Mn are stronger in the earlier study but the Pb risks are similar to the present findings.

In the present study, we find evidence that mortality risks associated with air pollution for this cohort have declined over time. This finding is also supported by the extant literature, notably Lipfert and Morris,[17] Enstrom,[18] and by the difference between the results of Pope et al.[12] for 1982-98 mortality and Pope et al.[13] for 1982-89 mortality. Further, Laden et al.[19] report the results of extended follow-up of the Six Cities Study, showing a decline in excess risk over time (1990-98 vs. 1974-89). Based on the original air quality data reported by Dockery et al.,[10] none of the all-cause mortality risks associated with SO_2, NO_2, or NO_x is significant in the later period, and the rate of risk decline for the group of pollutants is nearly significant (p=0.07). Jerrett et al.[20] reported additional analyses of the American Cancer Society CPS-II cohort,[12] and found that

cardiovascular mortality risks associated with sulfates declined from 1982-2000 while those associated with $PM_{2.5}$ increased. They attributed this trend to a shift in the composition of PM2.5 towards less sulfate and more traffic-related PM.

In conclusion, all of the traffic-related studies listed above[1-10] are in general agreement with the present study, by finding excess risks of similar magnitudes near roadways or associated with traffic-related pollutants, based on local impacts. There is also support for downward trends and the existence of thresholds (from roadway proximity studies). Several studies used dispersion modeling to estimate pollution exposures. The Six Cities Study[11] finds similar risk levels but cannot identify specific pollutants with certainty. The ACS[12-14] studies do not consider local or traffic impacts and their results differ from our findings, with the exception of SO_2.

References for Appendix C

1. Finkelstein, M.M., Jerrett, M., Sears, M.R. Traffic air pollution and mortality rate advancement periods; *Am J Epidemiol*. **2004,** *15*, 173-177.

2. Tonne, C., Melly, S., Mittleman, M., Coull, B., Goldberg, R., Schwartz, J. A case-control analysis of exposure to traffic and acute myocardial infarction; *Environ Health Perspect*. **2007**, *115*, 53-57.

3. Hoffmann, B., Moebus, S., Stang, A., Beck, E.M., Dragano, N., Mahlenkamp, S., Schmermund, A., Memmesheimer, M., Mann, K., Erbel, R., Jackel, K.H., Heinz Nixdorf RECALL Study Investigative Group. Residence close to high traffic and prevalence of coronary heart disease; *Eur Heart J*. **2006**, *27*, 2696-2702.

4. Gehring, U., Heinrich, J., Kraemer, U., Grote, V., Hochadel, M., Sugiri, D., Kraft, M., Rauchfuss. K., Eberwein, H.G., Wichmann, H.E. Long-term exposure to ambient air pollution and cardiopulmonary mortality in women; *Epidemiology* **2006,***17*, 545-551.

5. Rosenlund, M., Berglind, N., Pershagen, G., Hallqvist, J., Jonson, T., Bellander, T. Long-term exposure to urban air pollution and myocardial infarction; *Epidemiology*, ***2006,*** *17*, 383-390.

6. Elliott, P., Shaddick, G., Wakefield, J.C., de Hoogh, C., Briggs, D.J. Long-term associations of outdoor air pollution with mortality in Great Britain; *Thorax* **2007,** *62*,1088-1094.

7. Nafstad, P., Haheim, L.L., Wisloff, T., Gram, F., Oftedal, B., Holme, I., Hjerrman, I., Leren, P. Urban air pollution and mortality in a cohort of Norwegian men; Environ Health Perspect. **2004**, *112*, 610-615.

8. Naess, O., Nafstad, P., Aamodt, G., Claussen, B., Rosland, P. Relation between concentration of air pollution and cause-specific mortality: four-year exposures to nitrogen dioxide and particulate matter pollutants in 470 neighborhoods in Oslo, Norway; *Am J Epidemiol*. **2007**, *165*, 435-443.

9. Hoek, G., Brunekreef, B., Goldbohm, S., Fischer, P., van den Brandt, P. Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study; *Lancet* **2002**, *360*, 1203-1209.

10: Beelen R, Hoek G, van den Brandt PA, Goldbohm RA, Fischer P, Schouten LJ, Jerrett M, Hughes E, Armstrong B, Brunekreef B. Long-term effects of traffic-related air pollution on mortality in a Dutch cohort (NLCS-AIR study). Environ Health Perspect. 2008 Feb;116(2):196-202. Also see Beelen R, Hoek G, van den Brandt PA, Goldbohm RA, Fischer P, Schouten LJ, Armstrong B, Brunekreef B. Long-term exposure to traffic-related air pollution and lung cancer risk. Epidemiology. 2008 Sep;19(5):702-10.

11. Dockery, D.W., Pope, C.A. 3rd, Xu, X. Spengler, J.D., Ware, J.H., Fay, M.E., Ferris, B.G. jr., Speizer, F.E.., An association between air pollution and mortality in six US cities; *N Engl J Med.* **1993**; *329*, 1753-1759.

12. Pope, C.A. 3rd,Burnett, R.T., Thun, M.J., Calle, E.E., Krewski, D., Ito, K., Thurston, G.D. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution; *JAMA*. **2002**, *28*, 1132-1141.

13. Pope, C.A. 3rd, Thun, M.J., Namboodiri, M.M., Dockery, D.W., Evans, J.S., Speizer, F.E., Heath, C.W., Jr. Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults; *Am J Respir Crit Care Med.* **1995**, *151*, 669-674.

14. Krewski, D., Burnett, R.T., Goldberg, M.S., Hoover, K., Siemiatycki, J., Abrahamowicz, M., White, W.H., others. 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 Institute, **2000**. Part I. Replication and Validation (http://www.healtheffects.org/Pubs/Rean-part1.pdf) and Part II. Sensitivity Analyses (http://www.healtheffects.org/Pubs/Rean-part2.pdf).

15. Lipfert, F.W., Perry, H.M. Jr., Miller, J.P., Baty, J.D., Wyzga, R.E., Carmody, S.E.. The Washington Unversity-EPRI Veterans Cohort Mortality Study: preliminary results; *Inhal Toxicol.* **2000,** *12, Suppl 4*, 41-73.

16. Lipfert, F.W., Malone, R.G., Daum, M.L., Mendell, N.R., Yang, C-C. A Statistical Study of the Macroepidemiology of Air Pollution and Total Mortality; Report BNL-52122, Brookhaven National Laboratory, Upton, NY, April 1988.

17. Lipfert, F.W., Morris, S.C., Temporal and spatial relationships between age-specific mortality and ambient air quality in the United States: Preliminary results for counties, 1960-97; *Occup Env Med.* **2002**, *59*, 156-174.

18. Enstrom, J.E. Fine particulate air pollution and total mortality among elderly Californians, 1973-2002; *Inhal Toxicol.* **2005,** *17*, 803-816.

19. Laden, F., Schwartz, J., Speizer, F.E., Dockery, D.W. Reduction in fine particulate air pollution and mortality: Extended follow-up of the Harvard Six Cities study; *Am J Respir Crit Care Med*. **2006**, *173*, 667-672.

20. Jerrett, M., Newbold. K.B., Burnett, R.T., Thurston, G., Lall, R., Pope, C.A. III, Ma, R., De Luca, P., Thun, M., Calle, J., Krewski, D. Geographies of uncertainty in the health benefits of air quality improvements; *Stoch Environ Res Risk Assess* . **2007**, *21*, 511-522.

Table C-1 Comparison of All-Cause Mortality Risks in Selected US Cohort Studies, Based on Mean Concentrations

	SO_2	SO_4^{2-}	NO_2 or NO_x
Dockery et al. (Six Cities)*	1.12 (1.04-1.21)	1.24 (1.08-1.42)	1.26 (1.07-1.52)
Krewski et al. (orig ACS)**	1.084 (1.06-1.11)	1.063 (1.04-1.09)	0.97 (0.94-1.00)
Pope et al. (ACS CPS II)***	1.045 (1.02-1.07)	1.095 (1.04-1.15)	1.01 (0.97-1.05)
present study*** *	1.07 (1.06-1.085)	0.936 (0.91-0.96)	1.18 (1.17-1.20)

- based on Krewski et al.,[13] Part II, Table 16, adjusted to mean concentration levels.

** based on Krewski et al.,[13] Part II, Tables 31, 32, adjusted to mean concentration levels.

*** based on Figure 5 of Pope et al.,[11] using multi-year exposures. Mortality from 1982-98.

**** based on Table 5 of this study, for NO_x in high-traffic counties. Mortality from 1976-2001.

Appendix D. Supplementary Material on the Estimated Air Quality Data

1. Correlations with measured ambient air quality data.

The most relevant correlations are between like species, using data from previous publications on the Veterans Cohort. These results are listed in Table D-1; the weighted correlations are weighted by 1989 population. The strongest correlations are seen for sulfates (SO_4), especially for the IPN dataset, which was used in the ACS studies. The weakest relationships are seen for the more localized pollutants, such as SO_2, EC, and metals; this could be due to comparing the county-wide model estimates with local spot measurements. Correlations between measured NO_2 and predicted NO_x are influenced by the non linearity of this photochemical relationship.[1] The highest predicted NO_x values agree with the expected slope,[1] but many of the lower model estimates are substantially less than measured, especially in Southern California. Differences between county averages and local measurements could account for some of these differences.

Table D-1. Spatial correlations between measured ambient air quality indicators and AER or HAPS estimates.

		correlations		
Estimated parameter	measured parameter	unw't'd	weighted	#obs
A. AER estimates				
SO_4	1975-81 AIRS SO_4 (from TSP)	0.82	0.69	421
SO_4	STN SO_4 (from $PM_{2.5}$)	0.82	0.56	192
SO_4	ACS SO_4:(from TSP)	0.77	0.49	150
SO_4	IPN SO_4 (from $PM_{2.5}$)	0.85	0.83	75
NO_x	1975-81 AIRS NO_2	0.57	0.42	259
NO_x	1982-88 AIRS NO_2	0.61	0.43	234
NO_x	1989-96 AIRS NO_2	0.66	0.58	288
SO_2	1975-81 AIRS SO_2:	0.26	0.39	520
SO_2	1982-88 AIRS SO_2:	0.27	0.36	493
SO_2	1989-96 AIRS SO_2:	0.29	0.36	450
elemental carbon	STN elemental carbon	0.42	0.26	192
B. HAPS estimates				
nickel	STN nickel (from $PM_{2.5}$)	0.27	0.28	178
manganese	STN manganese (from $PM_{2.5}$)	0.01	0.04	178
lead	STN lead (from $PM_{2.5}$)	0.20	0.13	178
arsenic	STN arsenic (from $PM_{2.5}$)	-0.16	-0.28	178
chlorine	STN chloride (from $PM_{2.5}$)	0.24	0.13	178
average diesel PM	diesel traffic density	0.75	0.89	3078
local peak diesel PM	diesel traffic density	0.80	0.83	3078

acronyms ACS: American Cancer Society studies by Pope et al.
IPN: Inhalable Particulate Network.
AIRS: Aerometric Information Retrieval System (US EPA)
STN: Speciation Trends Network (US EPA)

2. Comparisons with Ambient Measurements in Bronx County, NY (FIPS 36005)

The South Bronx area of New York City has been identified as suffering from urban blight, poverty, and environmental injustice. It has one of the highest childhood asthma prevalence rates in the nation, heavy vehicular traffic, and various industrial facilities.

One of its major highways connects with the George Washington Bridge, which carries about 300,000 vehicles per day in 14 lanes of traffic. Bronx County has the nation's highest values for several of the air quality indicators considered in this study. Table D-2 compares those model estimates with the various measurements available from the literature, for similar time periods. Values are in $\mu g/m^3$ unless otherwise indicated.

Table D-2. Comparisons of ambient air quality estimates for Bronx County, NY

pollutant	this study	STN[2]	other studies
SO_2 (ppb)	19.2		17-20
SO_4^{2-}	6.2	4.1	4.1-4.3
NOx (ppb)	72.1		40 (as NO_2)
EC	3.5	1.3	2.7-4.4
benzene	3.2		1.1-2.7[7]
formaldehyde	5.1		4.7-8.6[7]
HCl	0.16		0.47
As	0.00022	0.0013	
Mn	0.0074	0.00020	
Ni	0.0053	0.021	
Pb	0.021	0.0061	

Some of these comparisons are quite good, while others are only approximate. Some of the other findings from the relevant literature are also worth mentioning. Carslaw et al.[1] presented measured data on the relationship between NO_x and NO_2 in London, for which a linear relationship with a slope of about 0.6 fits with an error of less than 1 ppb. On this basis, the measured NO_x value of 72 ppb in the Bronx would correspond to 43 ppb as NO_2, which compares quite well to actual measurements. The corresponding national average NO_2 value would be 12 ppb for all subjects in this cohort and 18.6 ppb for subjects in the high-traffic counties. The latter estimate comports well with the measured value (20 ppb) for the STN counties.[3]

Ito et al.[2] performed factor analyses on speciated $PM_{2.5}$ data from three monitors in Bronx and Queens Counties, NY. They found somewhat different factors at each station and concluded that the traffic factors were much less spatially correlated than the secondary aerosol factors. They concluded that "a source-oriented evaluation of PM health effects needs to take into consideration the uncertainty associated with spatial representative[ness] of the species measured at a single monitor."

Bari et al.[4] noted that HCl may be attributed to local as well as regional sources, with an estimated 27% from the latter (presumably midwestern coal burning). The ambient HCl estimates used in this analysis are presumably due only to local sources, which may help account for the lower values. Bari et al.[5] also noted similar patterns between ambient HCl and SO_4^{2-} in summer, when the highest concentrations occurred. Thus, SO_4^{2-} in the eastern US may be a crude proxy for HCl from regional sources.

Restrepo et al.[6] assessed the effect of sensor height above ground on ambient concentrations by comparing data obtained from a mobile lag at 4 m above ground with those monitored by the NYSDEC at 15 m above ground. NO_2 and CO levels were over twice as high at the lower elevations, while SO_2 was only higher at 4 m during August. Ozone levels were lower at 4 m and $PM_{2.5}$ levels were about the same. These data

suggest that routinely monitored ambient air quality data should be considered as indicators rather than actual exposures. Spatial differences in monitoring heights could easily confound spatial exposure patterns.

In summary, both local spot ambient measurements and dispersion model estimates entail uncertainties with regard to their interpretation as individual exposures.

3. Comparisons of HAPS model estimates with ambient measurements

The US EPA published a detailed critique of the 1996 NATA ambient concentration estimates, as compared to the available ambient measurements, for selected species[10] (hereafter, the "ASPEN" [Asessment System for Population Exposures Nationwide] report.) Among them, benzene, formaldehyde, lead, and diesel PM pertain to the current analysis. Data on SO_2 predictions were also presented in discussing the underlying dispersion model development. The emphasis throughout the ASPEN report is on predicting the magnitudes of specific exposures; no attention is given to the validity of the spatial distributions, which are more relevant to long-term epidemiology studies than the absolute values per se. Presenting risk estimates on the basis of mean concentrations (elasticities) precludes bias due to uncertainties in absolute values, since a high mean value will result in a lower risk coefficient and no effect on the elasticity. Long-term spatial distributions may be compared graphically or characterized in terms of spatial correlation coefficients (R or R^2). The only such correlations presented by EPA were for SO_2 or PM within specific metropolitan areas; R^2 values ranged from 0.90 to 0.96 for seven published modeling studies, even though as few as 40% of the model predictions were within 30% of the measured values. This indicates that it may be easier to predict the relative spatial patterns than the absolute concentrations.

The ASPEN report summary concludes the following:

> Modeled estimates are typically lower than measurements when compared at the exact monitor location. However, comparisons are better when maximum modeled concentrations are considered within about 30 km of the monitoring site. This lends credence to the use of county spatial averages in our analysis, based on the median level for the census tracts in the county. The ASPEN report attributed part of the local discrepancies to uncertainties in precise locations of emission sources.
>
> Among the species listed above, benzene had the best comparisons with measurements, with a median model/monitor concentration ratio of 0.92. Predictions were within 30% of measurements 59% of the time. Spatial correlations were not provided.
>
> Formaldehyde (outdoor) levels were systematically underestimated, and indoor exposures were not considered. The ASPEN report states that secondary reactions leading to aldehydes including formaldehyde were not considered.

Again, spatial correlations were not considered, but should not be greatly affected by *systematic* underestimation.

The largest problems were seen with particulate metal species, including lead, which was greatly underestimated in the ASPEN report, based largely on point-source monitors. However, comparing subject-weighted means from the STN network[11] with the NATA shows somewhat better comparisons (Table D-3, where values are in ng/m^3 except as shown). There are no direct ambient measurements of diesel PM (DPM), which is strongly associated with EC. The ASPEN report cites an EPA study[12] of this relationship, which finds ratios of either 2.0 or 1.3, depending on how EC is measured. Comparing averages of NATA diesel PM with AER EC in the current study shows a ratio of 2.16. The EPA report[12] cites overall DPM/$PM_{2.5}$ ratios of 0.091 for rural areas and 0.166 for urban areas (their Table 3-1). We find a ratio of 0.14 between NATA DPM and overall $PM_{2.5}$,[3] which agrees quite well.

Gray and Cass[13] studied these relationships in the Los Angeles basin and found good agreement between measured and modeled EC for seven locations (their Table 2). The correlation is 0.66 with a slope of 0.95. Their overall means agree quite well (3.88 vs.3.65 μg/m^3), but the modeled values are considerably more variable than the measurements. Note that these 1982 EC values are considerably higher than current levels.

Table D-3 Comparisons between measured values and NATA/AER estimates.

Species	STN mean	NATA or AER means	
		All subjects	**high-traffic counties**
As	1.67	0.15	0.20
Cl (1)	30.6	19.1	16.8
EC (2)	0.79	0.82	1.18
Mn	9.26	3.08	4.13
Ni	1.41	2.09	3.49
Pb	7.54	5.68	8.63
SO_4^{2-} (3)	3.90	4.28	6.37
Diesel PM (4)	1.58	1.81	2.53

(1) STN chloride is compared with NATA chlorine
(2) ASPEN also compares EC with diesel PM. The table shows AER EC (μg/m^3).
(3) The table shows AER SO_4^{2-} (μg/m^3).
(4) The table compares STN EC multiplied by 2.0 with NATA diesel PM (μg/m^3).

Table D-3 shows both over- and under-estimates, good agreement for EC and Pb, and reasonable agreement for Ni and SO_4^{2-}. This reinforces the conclusion that model-monitor comparisons can be sensitive to the selection of monitors. Overall, we find satisfactory agreement between key measured and modeled estimates of air quality parameters associate with vehicle emissions.

References Cited in Appendix D

1. Carslaw DC, Beevers SD, Fuller G. An empirical approach for the prediction of annual mean nitrogen dioxide concentrations in London, *Atmos Environ.* **2001,** *35*, 1505-1515.

2. Ito K, Xue N, Thurston G. Spatial variation of $PM_{2.5}$ chemical species and source-apportioned mass concentrations in New York City. *Atmos Environ,* **2004** *38*, 5269-5282.

3. Lipfert FW, Baty JD, Miller JP, Wyzga RE. $PM_{2.5}$ constituents and related air quality variables as predictors of survival in a cohort of U.S. military veterans. *Inhal Toxicol.* **2006,** *18*, 645-657.

4. Bari A, Ferraro V, Wilson LR et al. Measurements of HONO, HNO_3, SO_2, HCl, NH_3, particulate sulfate and $PM_{2.5}$ in New York, NY. *Atmos Environ.* **2003,** *37*, 2825-2835.

5. Bari A, Dutkiewicz VA, Judd CD et al., Regional sources of particulate sulfate, SO_2, $PM_{2.5}$, HCl, and HNO_3, in New York, NY. *Atmos Environ.* **2003,** *37*, 2837-2844.

6. Restrepo C, Zimmerman R Thurston G et al., A comparison of ground-level air quality data with New York State Department of Environmental Conservation monitoring stations in South Bronx, New York. *Atmos Environ.* **2004,** *38*, 5295-5204.

7. Sistla G, Aleksik N, A comparison of PAMS and air toxics measurements, *Atmos Environ.* **2007,** *41*, 5719-5731.

8. Maciejczyk PB, Offenberg JH, Clemente J et al., Ambient pollutant concentrations measured by a mobile laboratory in South Bronx, NY, *Atmos Environ.* **2004,** *38*, 5283-5294.

9. Rattigan OV, Hogefe O, Felton HD et al., Multi-year urban and rural semi-continuous $PM_{2.5}$ sulfate and nitrate measurements in New York state: Evaluation and comparison with filter based measurements, *Atmos Environ.* **2006,** *40 Suppl 2*,192-205.

10. http://www.epa.gov/ttn/atw/nata/mtom_pre.html (summary); http://www.epa.gov/ttn/atw/nata/draft6.html (complete report). Last updated Aug. 4, 2008. Accessed Aug. 13, 2008.

11. Lipfert, F.W., Baty, J.D., Miller, J.P., Wyzga, R.E.. $PM_{2.5}$ constituents and related air quality variables as predictors of survival in a cohort of U.S. military veterans; *Inhal Toxicol.* **2006,** *18*, 645-657.

12. ICF Consulting, Diesel PM Model-To-Measurement Comparison, Report EPA 420-D-02-004, October 2002.

13. Gray, H.A., Cass, G.R. Source contributions to atmospheric fine carbon particle concentrations; *Atmos Environ.* **1998,** *32*, 3805-3825.