APPENDIX AVAILABLE ON THE HEI WEB SITE

Research Report 177

National Particle Component Toxicity (NPACT) Initiative: Integrated Epidemiologic and Toxicologic Studies of the Health Effects of Particulate Matter Components

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Study 4. Mortality and Long-Term Exposure to $PM_{2.5}$ and Its Components in the American Cancer Society's CPS-II Cohort

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Appendix I. Total Risk Index Measures to Assess Effects of Multiple Particulate and Gaseous Air Pollutants

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TOTAL RISK IMPACT MEASURES TO ASSESS EFFECTS OF MULTIPLE PARTICULATE AND GASEOUS AIR POLLUTANTS

STATISTICAL CHALLENGES

A fundamental requirement of multi-pollutant analysis to evaluate the relative importance of various mixtures of air pollutants is to recognize the substantial and often complex correlation structures among the various pollutant compounds, gases, and sources. Even efforts to construct a mix of pollutants emitted by specific sources do not necessarily result in a mix of $PM_{2.5}$ components and sources that are fully orthogonal (i.e., distinct and uncorrelated), because of (for example) meteorological conditions that affect all sources similarly. Given the correlation between some pollutant concentrations, it is even difficult to confidently interpret the regression coefficient from a single-pollutant model because this single coefficient may reflect the incomplete but combined effects of multiple, correlated pollutants. These complex correlations among many pollutants make it even more difficult to interpret regression coefficients from multi-pollutant models. Including several pollutants in a model can result in various outcomes: (1) coefficients mostly unaffected by others (suggesting independent effects); (2) coefficients that retain the same sign (positive or negative), but are each smaller in size (suggesting that they are sharing the effect, or that they are both imperfect indicators of a true risk factor); or (3) coefficients that are highly unstable, with some becoming inflated and others becoming null or changing signs. Estimates of the standard errors of coefficients may also be inflated due to multi-colinearity. Basically, the individual risk coefficients of correlated variables (such as multiple pollutants) are not estimable in an unbiased way, but the linear combination of the coefficients *can* be reliably estimated, even if the individual variables are correlated with each other. So here we compare the combined effects estimates for the HR, or the Total Risk Index (TRI) for different model specifications (e.g. for a model with two pollutants vs. a model with one pollutant) in order to assess the change in effect produced by the addition of another pollutant variable to the model.

Thus, although coefficients from multi-pollutant models cannot provide reliable effect estimates for individual pollutants, we can test whether or not models with various *combinations* of pollutants provide significantly different estimates of the overall pollution-related TRI of mortality, as compared with the same model with only a single index of pollution. We can also conduct focused exploratory analyses regarding the combination of variables that significantly contribute to estimates of the TRI.

STATISTICAL APPROACH

Using the standard Cox model and our random effects Cox model as described in the previous section, we estimated the association between mortality from various causes and each pollutant, or set of pollutant variables, simultaneously. As in the single-pollutant mortality analyses, the model evaluates the survival data of CPS-II cohort members from 1982 through 2004; however, instead of estimating parameters for a single pollutant, the Cox models estimate vector parameters for the entire matrix of pollutants comprising the TRI .

To do this, we first defined the combined relative risk of a single pollution index or a set of pollutants, evaluated at their respective IQRs, denoted by the vector $\tilde{x}$. Let $\hat{\beta}$ represent the vector of estimated log–hazard ratios within the random effects Cox model structure associated with the multiple pollutant variables contained in the model, and let $\tilde{x}$ be a vector of the IQRs of the pollutant concentrations. The TRI of the set of pollutants is defined as: $TRI = \exp(\hat{\beta}\tilde{x})$ where the 95% CIs are given by $\exp\left(\hat{\beta}\tilde{x} \pm 1.96\sqrt{\tilde{x}'Cov(\hat{\beta})\tilde{x}}\right)$.

DATASETS

Cohort Mortality Data

Mortality data and personal-level covariate data were obtained from the American Cancer Society for their CPS-II cohort. Please see Tables 3 and 4 of Study 4 in the Investigator's Report for detailed descriptive information. For the TRI analysis, we analyzed mortality from all-causes and from cardiopulmonary diseases, cardiovascular disease, ischemic heart disease, and lung cancer. In this brief section, we focus on the IHD analysis.

Exposure Variables in TRI Formulation

The initial analysis of mortality associated with trace components, factors, and source-apportioned mass used data on $PM_{2.5}$ components derived from all sites that had both trace elements and "nearest neighbor" NO_2 data (n=212 sites). However, not all of the 100 MSAs where CSN monitoring occurred had the within-MSA NO_2 monitoring information required to identify a Traffic source category. For the TRI analyses, we conducted two new factor analyses and associated source-apportionment analyses — one based on the subset of 51 MSAs for which appropriate NO_2 data were available, and one for the remaining 49 MSAs for which $PM_{2.5}$ components alone were used. Source-apportioned mass variables were calculated from the factor scores from these new source apportionments as described in Study 4 of the Investigator's Report. Three important secondary aerosols (SO_4^{2-}, NO_3^-, and OC) make up a large proportion of $PM_{2.5}$ mass. However, we omitted them from the factor analysis so we could more clearly identify the primary emission sources of the measured $PM_{2.5}$ mass. Estimates of these residual secondary aerosols (i.e., "other" secondary aerosol not associated with a specific source) were also used to when subsequently constructing estimates of the total $PM_{2.5}$ mass associated with each source category (denoted in the initial analyses as source-apportioned mass).

These data and the factor analysis and source apportionment methods used to construct the source category variables are more completely described in Study 4 of the Investigator's Report. In our TRI analysis, we used the same data as we used in the cohort mortality analysis, but created multiple formulations for the TRI that were intended to represent complex atmospheres without duplicating the exposure data. We therefore created three different basic formulations of the TRI.

First, we computed TRIs for each of the health outcomes using $PM_{2.5}$ alone in order to compare our TRI results to conventional analyses and to other TRI formulations. Second, as our CSN data consisted of measurements of the components of $PM_{2.5}$ mass, we included TRI formulations with "components". These analyses used all of the following pollutants in the TRI formulation: $PM_{2.5}$ components known to be associated with specific source categories or their key tracers (i.e., Si/Soil, Zn/Metals, EC/Traffic, Cl/Salt, Ni/Residual Oil Combustion, Fe/Steel Industry, Se/Coal Combustion, and K/Biomass Combustion) other $PM_{2.5}$ constituents such as individual metals (As, Ca, Cu, Cl, Fe, Pb, Mn, Ni, Se, V, Si, Zn, K, and Na),), and OC and EC. We also estimated TRIs for our source categories, both in the form of factor scores (factors) and source-apportioned $PM_{2.5}$ mass (source mass).

To complete the characterization of the atmospheres for TRI analyses, we included the estimates of residual mass for SO_4^{2-}, OC, and NO_3^- (estimated via the APCA analysis described in the previous section) as variables in the TRI formulations. These "secondary" variables were included along with the variable sets for Source Mass, the Factors, or the Components in the mortality models. (For the set of Factors, we used normalized versions of mass for these three secondary aerosols.) Adding these "secondary" variables allowed us to more directly compare the multi-pollutant TRI with a TRI based on

$PM_{2.5}$ mass alone, as they are known to comprise the bulk of $PM_{2.5}$ mass. Using factor scores, we were able to calculate an IQR for the Steel Industry source category for some of the 100 MSAs in our study. We therefore included that source category in our "Factors" group in the TRI analyses. However, we were not able to calculate a non-zero IQR for the Steel Industry source category in any of our MSAs for the corresponding source-apportioned mass variable, and were thus unable to include the Steel Industry source category in our TRI calculations using "sources".

Gases were also considered in the TRI analyses. They were not part of the TRI formulations, but were included as a separate random variable in the Cox models in addition to the TRI. The results of these analyses are not included in this brief overview, but are presented in the online appendix. We thus examined 11 combinations of $PM_{2.5}$ mass Components, Factors, or Source categories in combination with Secondary Aerosols, with and without gaseous pollutant data, as shown in Table I.1.

Descriptive Statistics of Data Subsets

The medians and ranges of the individual pollution variables are presented in Table I.2 and the IQRs in Table I.3 for the various subsets of MSAs based on the available pollution data. In general, the $PM_{2.5}$ mass and component median concentrations were stable among the five subset databases; the only exception was for Pb in the subset of 45 MSAs with SO_2 data, which displays a lower value.

However, when these $PM_{2.5}$ component concentrations were used to generate Factors and Source-apportioned Mass Variables, some variation in medians was observed. In particular, for the Source-apportioned mass in the 51 MSAs for which within-city NO_2 data was incorporated into the source apportionment, the medians were different than those for the Source-apportioned mass in the other data subsets (see Table I.2). The limited availability of the NO_2 data may be related to differences in the source mixtures, and therefore differences in NO_2 concentration levels, with lower prevailing NO_2 levels not requiring monitoring in many MSAs. There is less variation in the IQRs of the Components compared with either the Factors or source-apportioned mass variables (see Table I.3).

HYPOTHESES TESTED

Our initial hypotheses are summarized here: The TRI based on the Source Categories set does not equal the TRI based on the Components set, which does not equal the TRI based on the Factors set, all of which are higher than the TRI based on $PM_{2.5}$ mass alone; or TRI (Source–apportioned Mass Variables) ≠ TRI ($PM_{2.5}$ Constituent Components) ≠ TRI (Factors) > TRI ($PM_{2.5}$ mass)

We tested the hypotheses that [1] the combination of all Source–apportioned mass variables or of all Factors represents the toxicity of an atmospheric mix differently than the combination of all selected Components; and [2] separating the set of Components from the sets of Source Categories and Factors provides a better representation of toxicity than a simple measure of $PM_{2.5}$ mass.

Note that, in order to avoid a multiple testing problem by which tests can be reported as significant just by chance alone, we included all source-apportioned mass variables or all source-related factors or all $PM_{2.5}$ trace element constituent components together as groups of variables in a single model, and not just those that had shown a statistically significant association with mortality when analyzed individually in our earlier analyses. (We refer to these as "sets".)

We also examined the influence on the TRI of the addition of a single gaseous pollutant (SO_2, NO_2, or O_3) to either $PM_{2.5}$ mass, or each set of Source Categories, Factors, or $PM_{2.5}$ Constituent Components. The key question asked in these comparisons was: Do the gases, either singly or in combination with these other pollution variables, meaningfully increase the TRI beyond that due to $PM_{2.5}$ mass alone? For example, hypotheses to be tested would include:

TRI (Source Mass + gas) ≠ TRI (Components + gas) ≠ TRI (Factors + gas) > TRI ($PM_{2.5}$ mass + gas) > TRI ($PM_{2.5}$ mass) ≠ TRI (gas) > TRI (NO_2) ≠ TRI (SO_2) ≠ TRI (O_3).

EFFECT MODIFICATION OF GASES

The above TRI analytic approach was designed to identify combinations of pollutants that would best represent the toxicity of the atmospheric mix; but it does not directly estimate the potential interaction of a gas with the particles or how that interaction might modify the effects of particle phase pollution. To assess the effect modification by gases, we postulated a model that included an interaction between a gas and the atmospheric composition of $PM_{2.5}$. We used a model in which each set of pollution variables [(1) $PM_{2.5}$ components, (2) Factors, or (3) Source-apportioned mass variables] was included along with a gaseous pollutant, and we measured the interaction of each set of the variables with the gaseous pollutant. Likelihood ratio tests were used to evaluate the strength of statistical evidence for such an interaction.

For those models in our initial analyses that had displayed strong evidence of an interaction ($P < 0.01$), we calculated a TRI based on three concentrations of the gaseous pollutant. These concentrations were determined by subdividing the MSAs with available data into three groups based on their concentration rankings. The three TRIs were calculated based on the formula:

$$TRI_i = \exp\left(\lambda G^{(i)} + \sum_{j=1}^{J} \beta_j \tilde{x}_j + \gamma_j G^{(i)} * \tilde{x}_j\right), \quad i = 1,2,3,$$

where λ is the regression coefficient associated with gas G, β_j is the regression coefficient of the jth main pollutant variable to which other variable will be added, γ_j is the regression coefficient of the interaction between the jth pollutant variable and G, $G^{(i)}$ is the average concentration of the ith tercile of the gas, and $\tilde{x}_j$ is the IQR of the jth set of Source Categories, Factors, or $PM_{2.5}$ Constituent Components.

Confidence Intervals for TRI Ratios of 3rd to 1st Quartiles

The addition of 25th and 75th percentile levels for all sets of the pollutant variables in a single TRI (using the IQR basis for models) may introduce bias because the highest and lowest values for all variables do not always occur in the same $PM_{2.5}$ samples at the same time. This potential scaling problem may make the TRI more difficult to interpret as a measure of comparative importance of different atmospheric mixes in assessing a mortality–pollution association. Therefore, we have also conducted sensitivity analyses of the TRI calculations on a subset of variables, wherein the IQR was defined for each individual cohort participant, rather than for each MSA, as had been done for the primary TRI approach described above.

In this case, the TRI was defined for the ith subject individually as

$$TRI_i = \exp(\hat{\beta}' x_i),$$

where $F(\hat{\beta})$ is the distribution of the TRI among subjects for a given $\hat{\beta}$. Also, let $r(\hat{\beta}) = Q_3(\hat{\beta}) / Q_1(\hat{\beta})$ be the ratio of the 3rd to 1st quartiles of $F(\hat{\beta})$. We thereby sought to estimate the uncertainty in $r(\hat{\beta})$. However, no closed form was available, and thus we estimated the uncertainty using simulation methods.

We assumed in this sensitivity analysis that $\hat{\beta} \sim MVN(\hat{\beta}, Cov(\hat{\beta}))$. We then created a realization (estimated value) of $r(\hat{\beta})$ for each draw from the multivariate normal (MVN) distribution and formed an empirical 95% confidence interval based on the 2.5 and 97.5 percentiles. We used 1000 draws (iterations) to form the uncertainty distribution for each estimate.

RESULTS OF TRI ANALYSES

Comparison Between Standard Cox and Random Effects Cox Models With and Without Ecologic Covariates

For all causes of death, CIs tended to be larger for the random effects model with ecologic covariates compared with the standard Cox model with or without ecologic covariates (see Figure I.1). The larger CIs were due primarily to the incorporation of spatial dependencies in the models. This result was also found in some of our earlier analyses of $PM_{2.5}$ mass (Krewski et al. 2009), as well as in the main mortality analyses reported in Study 4 of the main report. Differences in TRIs among model specifications, however, were not as consistent for cause-specific mortality analyses.

Interpretation of TRI Results

All Causes of Death (Table I.6)

The majority of TRIs for the set of Components alone were statistically significant at the 5% level.

The TRI based on $PM_{2.5}$ mass alone tended to be lower than the TRIs based on each set of Source-apportioned Mass variables, Factors, or Components alone. However, the CIs for the Source–apportioned Mass, Factor, and Component sets were wider than those for $PM_{2.5}$ mass alone. This is likely due to the large number of coefficients estimated for the TRI.

The TRI based on the set of Factors alone tended to be higher than the TRI based on the set of Source apportioned Mass variables alone, which was higher than the TRI based on the set of Components alone. There was less variation in the TRIs between the various combinations of variables used to characterize pollution in the atmosphere than between any given combination and the TRI for $PM_{2.5}$ mass alone.

The TRI including the set of Secondary Aerosols (SO_4^{2-}, NO_3^-, OC) was somewhat higher than the directly comparable TRI excluding the them, which provides suggestive evidence of a role for Secondary Aerosols in predicting all-cause mortality.

The evidence of an association between all causes of death and any of the three gases was weak; inferences are somewhat constrained by the more limited number of MSAs with gaseous data.

Cardiopulmonary Mortality (Table I.7)

Patterns of TRIs were similar to those for all causes of death, except that a positive and statistically significant association was seen between NO_2 alone and cardiopulmonary deaths. There was no evidence of an association with SO_2 or O_3.

The addition of NO_2 into the model increased the TRI for $PM_{2.5}$ mass; but had variable influence on the sets of Source-apportioned Mass variables and Factors depending on the set of MSAs included in the analysis. The interpretation of this model is complicated by the fact that both the Source-apportioned mass variable and Factor for the Traffic source category included NO_2.

CVD Mortality (Table I.5)

Patterns of TRIs were similar to those for cardiopulmonary mortality. This was not unexpected, since only a small number of respiratory deaths had occurred and the $PM_{2.5}$ mass association with respiratory mortality was weak in this cohort.

IHD Mortality (Table I.4)

Patterns of TRIs were observed that were similar to those for cardiopulmonary, cardiovascular, and all causes of death.

The TRIs for IHD deaths were generally higher than those for cardiovascular deaths, a pattern observed in previous analyses of this cohort (Pope et al. 2004; Krewski et al. 2009). The TRIs based on the Factors set, and especially when Secondary Aerosols were included, were substantially larger than the TRIs based on $PM_{2.5}$ mass alone. For example, in Table I.4, the TRI estimate for the random effects model with ecologic covariates is 1.028 for $PM_{2.5}$ mass alone, 1.135 for Factors, and 1.173 for Factors + Secondary aerosols.

The TRI for IHD from the random effects model for NO_2 alone was significant (TRI = 1.046), which is consistent with an effect by Traffic-related pollution.

Unexpectedly, SO_2 alone was positive and significantly related to IHD mortality (TRI = 1.072), although smaller than for the $PM_{2.5}$ source factors and constituent components. This result is difficult to interpret, since no association with SO_2 was observed with cardiovascular mortality (TRI = 1.002; Table I.5), which implies a negative association between SO_2 and other cardiovascular deaths, the majority of which were due to stroke. However, in the initial mortality analyses, the Coal Combustion factor and source-apportioned mass variable, which were among the most strongly correlated with SO_2 (see Thurston et al. 2011), were also important predictors of IHD (see Figures 10 and 11 in the main text of the Investigators' Report).

TRIs were generally much lower in the subset of 45 MSAs for which we had SO_2 data. This makes it difficult to interpret the joint impact of SO_2 and $PM_{2.5}$ mass (TRI = 1.075). Distinguishing the effects of data availability by MSA from a pollutant's impact on the TRI estimate is challenging when different pollutants are available in different MSAs.

Lung Cancer Mortality (Table I.8)

The Source-apportioned mass variable and Factor and sulfur were all associated with lung cancer mortality in the 100-MSA dataset. In the subset of MSAs with gaseous data, however, it is not clear whether the set of Components, or the sets of Source Categories or Factors based on them, were related to lung cancer mortality. In our initial mortality analyses, we observed a strong association between the Coal Combustion source category and lung cancer mortality. The Coal Combustion source category is also related to S; therefore it appears that inclusion of the other non-associated sources into the model was masking the link with the Coal Combustion source category. None of the gaseous pollutants alone, including NO_2, were related to lung cancer mortality.

Evaluation of Particle–Gas Interaction

We did not evaluate particle–gas interactions for either SO_2 or O_3. O_3 was not related to all-cause mortality or any of the specific causes of death in our TRI analyses; and although SO_2 was significantly related to IHD mortality in the TRI analyses, neither $PM_{2.5}$ mass, Source Categories, or Factors alone were related overall to IHD mortality in the 45 MSAs with SO_2 information (Table I.4).

We did examine the interaction of NO_2 with $PM_{2.5}$ mass, and of NO_2 with the set of Factors both with and without the set of Secondary Aerosols for CVD (Table I.5) and IHD mortality (Table I.4). (NO_2 was not clearly associated with all-cause mortality [Table I.6], and was more weakly associated with cardiopulmonary mortality [Table I.7] than with CVD mortality.)

Also, we examined an NO_2–$PM_{2.5}$ mass interaction with the sets of Source-apportioned Mass variables, Factors, or Components only if the TRI based on a model with any one of those variable sets and NO_2 was statistically significant in the earlier set of TRI analyses (i.e., $P < 0.05$). $PM_{2.5}$ mass and Factors (either with or without the Metals category) met these criteria. (In the earlier set of TRI analyses, the Source-apportioned Mass TRI was greater than unity, but not significant; and the Components TRI was less than unity and not significant in the subset of MSAs with NO_2 data.)

For the interaction between NO_2 and particulate pollution, in Table I.9 the Wald-test value for significance tended to be higher for the standard Cox model than for the random effects Cox model. This was expected since the random effects model incorporated additional variability in survival among the MSAs, which raises overall statistical uncertainty.

When testing both CVD and IHD mortality for the interaction between NO_2 and Factors, the strength of evidence of an interaction was greater (smaller *P* values) for the TRI for Factors plus the Secondary Aerosols than for Factors alone. The TRIs tended to increase with increasing NO_2 concentrations (analyses were based on terciles of NO_2 concentration), suggesting a potentiation of the toxicity of the particulate component of the atmosphere in areas of higher ambient concentrations of NO_2. (Note that these TRIs are not directly comparable to the TRIs reported in Tables I.4 and I.8 since those TRIs were based on an NO_2 IQR of 6.8 ppb and these are based on NO_2 terciles.)

To further interpret the NO_2–Factor interaction, the correlations between NO_2 and the individual components or the individual factors are presented in Table I.10. NO_2 was most positively correlated with the components EC, Cu, and Fe. It was most positively correlated with the Traffic factor, least correlated with the Biomass Combustion factor, and most negatively correlated with the Coal Combustion and Metals factors. NO_2 was positively correlated NO_3^- and OC but negatively correlated with SO_4^{2-}.

TRI Scaling

In Table I.4, we presented the TRI estimates based on the IQR of each set of variables that comprised a specific TRI formulation. We were particularly interested in comparing the TRI based on the different sets of variables (e.g. components, factors, or source mass) with that based on $PM_{2.5}$ mass alone. However, we found that a TRI based on $PM_{2.5}$ mass alone was consistently lower than the TRIs based on the sets of $PM_{2.5}$ Components, Source–apportioned Mass, or Factors. Using the IQRs may have overstated the magnitude of the TRI when the sum of the various Component IQRs that were used to calculate the TRI was much higher than the IQR for $PM_{2.5}$ Mass, as we found in these TRI analyses. Thus, it is not certain which are the most appropriately scaled values (e.g., IQR or other) for the variables when the goal is to compare multipollutant models using TRI formulations.

We therefore investigated an alternative method of evaluating TRIs, in which the TRI is determined based on each cohort subject's exposure values for each set of variables used in a TRI formulation. We hypothesized that, if a representation of the atmospheric mix appears to be toxic to human health, the distribution of subject-specific TRIs based on that representation (i.e., $PM_{2.5}$ mass, or a set of Components, Source–apportioned Mass variables, or Factors) will be more dispersed. That is, the TRIs associated with that representation will fall in a wider range, but one that is more representative of our cohort's exposure to multiple pollutants.

These results are consistent with the results from the mortality analyses with TRIs based on pollutant IQRs, but have hazard ratios and confidence intervals that are shifted to lower values. Both methods indicate higher TRIs for the various $PM_{2.5}$ component and source-related groups than for $PM_{2.5}$ mass.

Thus, even considering the uncertainties around these estimates, it does appear that, for both CVD and IHD, the association of the mixture yielded a larger impact on mortality than $PM_{2.5}$ mass alone.

To illustrate the subject-based TRI approach and to assess whether similar results are found by the two methods, we again used the standard Cox and random effects Cox models to develop TRIs for CVD and IHD mortality. Sets of variables for the TRI formulations included $PM_{2.5}$ mass, all eight Factors (as a set) with and without the set of Secondary Aerosols, and seven Factors (as a set; no Metals) with and without Secondary Aerosols. To examine again the NO_2—Factor interactions, to the $PM_{2.5}$ and set of Factors we added NO_2 plus NO_2—Factor interactions.

In Table I.11, we present the standard deviations of the subject-based TRI distributions, along with the ratios of the 3rd-to-1st quartiles (including the ratios' uncertainties) as additional representative measures of dispersion. For cardiovascular and IHD mortality, both the standard deviation and the TRI distribution IQR are larger for the Factors representation of the atmospheric mix than those for $PM_{2.5}$ mass alone. These results are consistent with the TRIs evaluated for the estimates made from the pollutant IQRs, but have lower values. It is not clear how to determine an uncertainty in either the standard deviation or TRI distribution IQR, and thus we cannot judge whether the greater toxicity implied by the Factors representation of the atmospheric mix is statistically different than that based on $PM_{2.5}$ mass alone. However, both methods indicate higher TRIs for the various $PM_{2.5}$ component and source-related groups than for $PM_{2.5}$ mass. Thus, even considering the uncertainties around these estimates, it does appear that, for both CVD and IHD, the association of the mixture yielded a larger impact on mortality than $PM_{2.5}$ mass alone.

CONCLUSIONS

The TRIs based on the source-related factors (and especially with the secondary $PM_{2.5}$ constituents also included) were generally larger than the TRI based on $PM_{2.5}$ mass alone, suggesting that the source-specific information allows for a more accurate exposure and risk estimate, and that past estimates using non-specific $PM_{2.5}$ mass alone may have provided underestimates of the total $PM_{2.5}$ mortality effect.

The TRIs including the secondary $PM_{2.5}$ constituents (SO_4^{2-}, NO_3^-, OC) tended to be somewhat larger than the directly comparable TRI excluding the secondary $PM_{2.5}$ constituents, providing evidence consistent with a contribution by secondary $PM_{2.5}$ constituents to $PM_{2.5}$ associations with mortality.

The evidence of an association for mortality with any of the three gaseous pollutants examined over and above that from $PM_{2.5}$ mass (and its components) was generally weak, although inferences are somewhat constrained by more limited number of MSAs.

Table I.1. Basic Design of TRI Analysis Formulation

$PM_{2.5}$ Mass and Sets of Factors, Components, and Source Mass	Secondary Aerosols	With or Without Metals Factor	Number of MSAs
$PM_{2.5}$ alone			100
Components			100
Components	Yes		100
Source Mass		With	100
Source Mass	Yes	With	100
Source Mass		Without	51 with NO_2 data
Source Mass	Yes	Without	51 with NO_2 data
Factors		With	100
Factors	Yes (normalized)	With	100
Factors		Without	51 with NO_2 data
Factors	Yes (normalized)	Without	51 with NO_2 data

Table I.2. $PM_{2.5}$ Mass and Individual Source Mass, Factors, Components, Gases, and Secondary Aerosols by Subset of MSAs[a]

Pollutant Variable	Median and Range for MSA Subset: 100 (445,860)	45 (SO_2) (240,692)	51 (NO_2) (289,522)	68 (O_3) (343,638)
$PM_{2.5}$ Mass	14.5676 (8.1831–26.4781)	14.3138 (8.5436–26.4781)	14.5676 (8.5436–26.4781)	14.5676 (8.5436–26.4781)
Source Mass				
Soil	0.6930 (0.1115–3.2451)	0.5946 (0.1115–2.9582)	0.5946 (0.1115–2.9582)	0.6004 (0.1115–2.9582)
Metals	0.1087 (0.0000–3.3707)	0.0840 (0.0000–1.1849)	0.0826 (0.0000–1.1849)	0.0840 (0.0000–3.3707)
Traffic	5.2349 (1.3963–12.4332)	5.6157 (1.3963–12.4332)	5.4614 (1.5972–12.4332)	5.4614 (1.3963–12.4332)
Salt	0.0800 (0.0000–0.8293)	0.0925 (0.0000–0.4610)	0.0812 (0.0010–0.7104)	0.0950 (0.0010–0.7104)
Residual Oil Combustion	0.6949 (0.0000–5.6157)	0.7032 (0.0000–5.6157)	0.7826 (0.0000–5.6157)	0.7393 (0.0000–5.6157)
Steel	0.0000 (0.0000–1.6887)	0.0000 (0.0000–0.2986)	0.0000 (0.0000–0.2986)	0.0000 (0.0000–1.6887)
Coal Combustion	0.8756 (0.0000–12.3304)	0.8595 (0.0432–12.3304)	0.8756 (0.0364–12.3304)	0.8756 (0.0000–12.3304)
Biomass Combustion	1.2436 (0.0000–7.6817)	1.2688 (0.0000–7.6817)	1.2688 (0.0000–7.6817)	1.2688 (0.0000–7.6817)
SO_4^{2-}	4.0218 (0.0000–7.3238)	3.6645 (0.0000–6.9483)	3.6782 (0.0000–6.9097)	3.9104 (0.0000–7.1439)
OC	0.0000 (0.0000–3.1854)	0.0000 (0.0000–2.5361)	0.0000 (0.0000–3.1854)	0.0000 (0.0000–3.1854)
NO_3^-	0.3171 (0.0000–9.4188)	0.1832 (0.0000–9.4188)	0.1832 (0.0000–9.4188)	0.1832 (0.0000–9.4188)
Factors				
Soil	−0.1278 (−0.4475 to 1.9491)	−0.1410 (−0.4284 to 1.5921)	−0.1410 (−0.4475 to 1.5921)	−0.1410 (−0.4475 to 1.5921)
Metals	−0.0410 (−0.4181 to 1.6350)	−0.0410 (−0.3194 to 0.6621)	−0.0696 (−0.3194 to 0.6621)	−0.0484 (−0.3194 to 1.6350)
Traffic	−0.1855 (−0.8301 to 2.1326)	0.3877 (−0.8301 to 2.1326)	0.3742 (−0.6824 to 2.1326)	0.3123 (−0.8301 to 2.1326)
Salt	−0.1168 (−0.5762 to 1.3218)	−0.0761 (−0.3480 to 0.5337)	0.1087 (−0.2858 to 1.1472)	−0.1165 (−0.3527 to 1.1472)
Residual Oil Combustion	−0.1886 (−0.6320 to 2.4428)	−0.1712 (−0.5192 to 2.4428)	−0.1366 (−0.5544 to 2.4428)	−0.1886 (−0.6320 to 2.4428)
Steel	−0.0397 (−0.3701 to 1.6085)	−0.0182 (−0.2506 to 0.5018)	−0.0285 (−0.2506 to 0.5018)	−0.0285 (−0.3701 to 1.6085)
Coal Combustion	−0.0160 (−0.4354 to 1.7717)	−0.0275 (−0.3191 to 1.7717)	−0.0275 (−0.4354 to 1.7717)	−0.0275 (−0.4354 to 1.7717)
Biomass Combustion	−0.0014 (−0.4784 to 1.1789)	0.0695 (−0.4706 to 0.7124)	0.0695 (−0.4706 to 0.7124)	−0.0107 (−0.4784 to 0.7124)

Table continues next page

[a] Values are in µg/m^3 for $PM_{2.5}$ and secondary aerosols, ng/m^3 for other components, and ppb for gases. Data are presented by number of MSAs with number of CPS-II cohort subjects in each MSA subset: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data available; 51 MSAs with local NO_2 data available; and 68 MSAs with O_3 data available.

Table I.2 (*Continued*). $PM_{2.5}$ Mass and Individual Source Mass, Factors, Components, Gases, and Secondary Aerosols by Subset of MSAs[a]

Pollutant Variable	Median and Range for MSA Subset: 100 (445,860)	45 (SO_2) (240,692)	51 (NO_2) (289,522)	68 (O_3) (343,638)
Factors (*Continued*)				
SO_4^{2-}	0.1369 (−0.9196 to 0.6912)	0.0142 (−0.7398 to 1.0873)	0.0142 (−0.7398 to 1.6292)	−0.0043 (−0.7398 to 1.6292)
OC	−0.0043 (−0.7398 to 1.6292)	0.1084 (−0.4703 to 3.0535)	0.0503 (−0.4731 to 3.0535)	0.0503 (−0.5202 to 3.0535)
NO_3^-	0.0399 (−0.5202 to 3.0535)	0.0132 (−0.7834 to 0.6203)	0.0662 (−0.7834 to 0.6203)	0.1112 (−0.7834 to 0.6203)
Components				
As	0.0013 (0.0006–0.0037)	0.0011 (0.0007–0.0026)	0.0011 (0.0006–0.0026)	0.0012 (0.0006–0.0037)
Ca	0.0578 (0.0167–0.3215)	0.0626 (0.0207–0.1659)	0.0587 (0.0181–0.1659)	0.0545 (0.0181–0.1659)
Cu	0.0040 (0.0009–0.0117)	0.0042 (0.0014–0.0117)	0.0041 (0.0014–0.0117)	0.0041 (0.0014–0.0117)
Cl	0.0264 (0.0032–0.2513)	0.0391 (0.0048–0.1166)	0.0338 (0.0048–0.1166)	0.0299 (0.0048–0.1166)
Fe	0.0904 (0.0263–0.2631)	0.0967 (0.0382–0.2595)	0.0910 (0.0373–0.2595)	0.0910 (0.0373–0.2439)
Pb	0.0040 (0.0016–0.0274)	0.0015 (0.0020–0.0153)	0.0045 (0.0020–0.0153)	0.0045 (0.0020–0.0274)
Mn	0.0024 (0.0010–0.0531)	0.0031 (0.0010–0.0100)	0.0026 (0.0013–0.0100)	0.0025 (0.0010–0.0531)
Ni	0.0012 (0.0002–0.0169)	0.0016 (0.0004–0.0169)	0.0013 (0.0002–0.0169)	0.0012 (0.0002–0.0169)
Se	0.0012 (0.0005–0.0058)	0.0011 (0.0005–0.0058)	0.0011 (0.0005–0.0058)	0.0011 (0.0005–0.0058)
V	0.0016 (0.0007–0.0105)	0.0017 (0.0007–0.0080)	0.0017 (0.0007–0.0080)	0.0017 (0.0007–0.0080)
Si	0.0893 (0.0418–0.3938)	0.0877 (0.0531–0.3938)	0.0893 (0.0418–0.3938)	0.0893 (0.0418–0.3938)
Zn	0.0138 (0.0043–0.1367)	0.0150 (0.0045–0.0459)	0.0141 (0.0043–0.0459)	0.0141 (0.0043–0.1367)
K	0.0649 (0.0346–0.1630)	0.0649 (0.0362–0.1227)	0.0649 (0.0362–0.1263)	0.0649 (0.0362–0.1263)
Na	0.0531 (0.0259–0.2649)	0.0596 (0.0263–0.1848)	0.0545 (0.0316–0.2649)	0.0540 (0.0316–0.2649)
Mg	0.0075 (0.0032–0.0231)	0.0076 (0.0032–0.0178)	0.0075 (0.0032–0.0231)	0.0075 (0.0032–0.0231)
EC	0.7052 (0.2356–1.5515)	0.7582 (0.3023–1.5515)	0.7582 (0.3023–1.5515)	0.7174 (0.3023–1.5515)
SO_4^{2-}	1.3589 (0.2632–1.9043)	1.2503 (0.3994–1.9043)	1.3131 (0.3994–1.9043)	1.3411 (0.3994–1.9043)
OC	4.1778 (2.4834–8.0443)	4.1778 (2.4834–6.7771)	4.1522 (2.4834–8.0443)	4.1973 (2.4834–8.0443)
NO_3^-	1.9959 (0.4279–10.6011)	2.2149 (0.5605–10.6011)	2.0759 (0.4865–10.6011)	2.0320 (0.4279–10.6011)

Table continues next page

[a] Values are in μg/m^3 for $PM_{2.5}$ and secondary aerosols, ng/m^3 for other components, and ppb for gases. Data are presented by number of MSAs with number of CPS-II cohort subjects in each MSA subset: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data available; 51 MSAs with local NO_2 data available; and 68 MSAs with O_3 data available.

Table I.2 (*Continued*). $PM_{2.5}$ Mass and Individual Source Mass, Factors, Components, Gases, and Secondary Aerosols by Subset of MSAs[a]

Pollutant Variable	Median and Range for MSA Subset			
	100 (445,860)	45 (SO_2) (240,692)	51 (NO_2) (289,522)	68 (O_3) (343,638)
Gases				
SO_2	—	3.2749 (0.2687–12.4235)	—	—
NO_2	—	—	19.1725 (6.1059–34.0479)	—
O_3	—	—	—	46.3659 (28.2044–66.1609)

[a] Values are in µg/m^3 for $PM_{2.5}$ and secondary aerosols, ng/m^3 for other components, and ppb for gases. Data are presented by number of MSAs with number of CPS-II cohort subjects in each MSA subset: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data available; 51 MSAs with local NO_2 data available; and 68 MSAs with O_3 data available.

Table I.3. Magnitude of IQRs for $PM_{2.5}$ Mass and Individual Source Mass, Factors, Components, Gases, and Secondary Aerosols by Subset of MSAs[a]

Pollutant Variable	100 MSAs	45 MSAs (SO_2)	51 MSAs (NO_2)	68 MSAs (O_3)
$PM_{2.5}$ Mass	3.00686	3.22618	3.00303	3.00303
Source Mass				
Soil	0.66562	0.66319	0.66822	0.71378
Metals	0.20613	0.16268	0.14983	0.17833
Traffic	3.11081	2.65754	2.52973	2.78812
Salt	0.10040	0.10594	0.10594	0.10594
Residual oil combustion	1.05964	1.28122	1.20709	1.14942
Steel	0.00	0.00	0.00	0.00
Coal combustion	0.71837	0.76493	0.74161	0.70910
Biomass combustion	0.59997	0.56454	0.56836	0.53964
SO_4^{2-}	2.74528	2.16919	3.04778	2.65622
OC	0.43242	0.08169	0.16147	0.30069
NO_3^-	1.26909	1.36006	1.26909	1.26909
Factors				
Soil	0.42690	0.44499	0.44877	0.44877
Metals	0.20535	0.17144	0.16064	0.23050
Traffic	0.64086	0.57286	0.49862	0.64420
Salt	0.21363	0.21112	0.22291	0.23499
Residual oil combustion	0.57469	0.87307	0.68213	0.60061
Steel	0.09990	0.10865	0.09324	0.09833
Coal combustion	0.25888	0.31067	0.38464	0.33656
Biomass combustion	0.20620	0.28260	0.26374	0.20845
SO_4^{2-}	0.50009	0.38892	0.51152	0.50093
OC	0.41267	0.45422	0.51180	0.44973
NO_3^-	0.50630	0.50409	0.50409	0.52757

Table continues next page

[a] IQRs are shown in μg/m^3 for $PM_{2.5}$ and secondary aerosols, ng/m^3 for other components, and ppb for gases; factors are unitless. Data are presented by number of MSAs: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data available; 51 MSAs with local NO_2 data available; and 68 MSAs with O_3 data available.

Table I.3 (*Continued*). Magnitude of IQRs for $PM_{2.5}$ Mass and Individual Source Mass, Factors, Components, Gases, and Secondary Aerosols by Subset of MSAs[a]

Pollutant Variable	100 MSAs	45 MSAs (SO_2)	51 MSAs (NO_2)	68 MSAs (O_3)
Components				
As	0.00055	0.00043	0.00043	0.00048
Ca	0.04382	0.04370	0.04370	0.04382
Cu	0.00245	0.00261	0.00226	0.00224
Cl	0.03350	0.03712	0.02677	0.03167
Fe	0.04775	0.04418	0.03789	0.03704
Pb	0.00259	0.00238	0.00248	0.00282
Mn	0.00207	0.00270	0.00281	0.00283
Ni	0.00145	0.00188	0.00187	0.00174
Se	0.00081	0.00069	0.00078	0.00073
V	0.00263	0.00365	0.00324	0.00317
Si	0.04288	0.04260	0.06791	0.05494
Zn	0.01013	0.01322	0.01342	0.01473
K	0.02186	0.02567	0.02657	0.02140
Na	0.03337	0.03528	0.03551	0.03567
Mg	0.00441	0.00497	0.00513	0.00544
EC	0.25755	0.41339	0.38658	0.33789
SO_4^{2-}	0.52882	0.41175	0.52252	0.51866
OC	0.98385	1.10339	1.21076	1.06665
NO_3^-	1.49123	1.40411	1.40411	1.52515
Gases				
SO_2	—	3.13391	—	—
NO_2	—	—	6.80303	—
O_3	—	—	—	4.34993

[a] IQRs are shown in μg/m^3 for $PM_{2.5}$ and secondary aerosols, ng/m^3 for other components, and ppb for gases; factors are unitless. Data are presented by number of MSAs: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data available; 51 MSAs with local NO_2 data available; and 68 MSAs with O_3 data available.

Table I.4. TRIs for IHD Mortality for Combinations of $PM_{2.5}$ Mass and Sets of Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Sets of Variables in TRI Formulation	Standard Cox Model		Random Effects Cox Model	
	Without Ecologic Covariates	With Ecologic Covariates	Without Ecologic Covariates	With Ecologic Covariates
100 MSAs (445,860 Subjects)				
$PM_{2.5}$ mass	1.041 (1.029–1.054)	1.018 (1.005–1.032)	1.046 (1.016–1.077)	1.028 (1.000–1.056)
Source mass	1.150 (1.116–1.186)	1.083 (1.044–1.124)	1.151 (1.073–1.234)	1.112 (1.038–1.192)
Factors	1.165 (1.132–1.199)	1.111 (1.072–1.152)	1.152 (1.082–1.226)	1.135 (1.067–1.208)
Components	1.085 (1.044–1.128)	1.048 (1.006–1.091)	1.101 (1.026–1.182)	1.069 (1.010–1.130)
Source mass + secondary aerosols	1.178 (1.131–1.227)	1.078 (1.022–1.137)	1.173 (1.072–1.282)	1.121 (1.018–1.233)
Factors + secondary aerosols	1.194 (1.151–1.238)	1.143 (1.092–1.196)	1.181 (1.100–1.268)	1.173 (1.092–1.260)
Components + secondary aerosols	1.120 (1.068–1.174)	1.063 (1.010–1.118)	1.150 (1.063–1.245)	1.097 (1.025–1.174)
45 MSAs with SO_2 Data (240,692 Subjects)				
SO_2	1.069 (1.048–1.090)	1.078 (1.046–1.112)	1.078 (1.022–1.138)	1.072 (1.027–1.120)
$PM_{2.5}$ mass	1.054 (1.039–1.069)	1.012 (0.990–1.034)	1.067 (1.023–1.113)	1.024 (0.983–1.066)
Source mass	1.167 (1.101–1.237)	0.988 (0.904–1.079)	1.208 (1.040–1.402)	1.018 (0.903–1.147)
Factors	1.074 (1.018–1.134)	1.020 (0.952–1.093)	1.138 (1.016–1.275)	1.020 (0.952–1.093)
Components	0.958 (0.885–1.037)	0.989 (0.903–1.085)	1.004 (0.905–1.115)	0.989 (0.903–1.085)
$PM_{2.5}$ mass + SO_2	1.115 (1.089–1.142)	1.076 (1.040–1.112)	1.129 (1.065–1.198)	1.075 (1.024–1.130)
Source mass + SO_2	1.215 (1.143–1.290)	0.994 (0.910–1.087)	1.244 (1.076–1.438)	1.005 (0.911–1.109)
Factors + SO_2	1.081 (1.022–1.144)	1.030 (0.958–1.107)	1.159 (1.031–1.302)	1.030 (0.958–1.108)
Components + SO_2	1.007 (0.923–1.099)	1.015 (0.920–1.119)	1.049 (0.943–1.167)	1.015 (0.920–1.119)

Table continues next page

[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.4 (*Continued*). TRIs for IHD Mortality for Combinations of $PM_{2.5}$ Mass and Sets of Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Sets of Variables in TRI Formulation	Standard Cox Model: Without Ecologic Covariates	Standard Cox Model: With Ecologic Covariates	Random Effects Cox Model: Without Ecologic Covariates	Random Effects Cox Model: With Ecologic Covariates
51 MSAs with NO_2 Data (289,522 Subjects)				
NO_2	1.027 (1.013–1.042)	1.039 (1.018–1.062)	1.013 (0.967–1.062)	1.046 (1.002–1.092)
$PM_{2.5}$ mass	1.045 (1.031–1.059)	1.013 (0.995–1.031)	1.048 (1.010–1.087)	1.022 (0.987–1.059)
Source mass	1.122 (1.065–1.182)	1.004 (0.933–1.081)	1.128 (0.989–1.286)	1.086 (0.957–1.232)
Factors	1.125 (1.072–1.181)	1.098 (1.034–1.165)	1.140 (1.028–1.264)	1.142 (1.044–1.249)
Components	0.987 (0.916–1.063)	0.927 (0.850–1.011)	1.011 (0.901–1.134)	0.927 (0.850–1.011)
$PM_{2.5}$ mass + NO_2	1.050 (1.034–1.068)	1.038 (1.015–1.063)	1.042 (0.992–1.096)	1.049 (1.002–1.098)
Source mass + NO_2	1.122 (1.065–1.182)	1.004 (0.932–1.082)	1.129 (0.993–1.285)	1.088 (0.965–1.227)
Factors + NO_2	1.129 (1.075–1.186)	1.092 (1.027–1.160)	1.135 (1.023–1.260)	1.134 (1.036–1.241)
Components + NO_2	0.926 (0.852–1.006)	0.945 (0.860–1.039)	0.963 (0.856–1.085)	0.946 (0.860–1.039)
68 MSAs with O_3 Data (343,638 Subjects)				
O_3	0.999 (0.990–1.008)	0.974 (0.963–0.986)	1.018 (0.995–1.040)	0.985 (0.963–1.008)
$PM_{2.5}$ mass	1.039 (1.025–1.053)	1.014 (0.997–1.031)	1.041 (1.007–1.076)	1.020 (0.987–1.054)
Source mass	1.116 (1.066–1.186)	1.024 (0.959–1.094)	1.136 (1.019–1.265)	1.097 (0.977–1.231)
Factors	1.137 (1.087–1.189)	1.117 (1.055–1.182)	1.142 (1.043–1.250)	1.164 (1.065–1.272)
Components	1.018 (0.957–1.084)	0.997 (0.936–1.062)	1.072 (0.966–1.191)	1.023 (0.949–1.103)
$PM_{2.5}$ mass + O_3	1.034 (1.020–1.050)	0.993 (0.975–1.012)	1.044 (1.009–1.080)	1.007 (0.973–1.043)
Source mass + O_3	1.117 (1.067–1.168)	1.043 (0.976–1.115)	1.134 (1.017–1.264)	1.103 (0.983–1.236)
Factors + O_3	1.123 (1.070–1.178)	1.092 (1.029–1.159)	1.149 (1.045–1.263)	1.148 (1.045–1.261)
Components + O_3	1.009 (0.948–1.074)	0.994 (0.932–1.060)	1.068 (0.965–1.183)	1.020 (0.946–1.100)

Table continues next page

[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.5. TRIs for CVD Mortality for Combinations of $PM_{2.5}$ Mass and Sets of Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Sets of Variables in TRI Formulation	Standard Cox Model		Random Effects Cox Model	
	Without Ecologic Covariates	With Ecologic Covariates	Without Ecologic Covariates	With Ecologic Covariates
100 MSAs (445,860 Subjects)				
$PM_{2.5}$ mass	1.030 (1.021–1.039)	1.027 (1.017–1.037)	1.028 (1.008–1.048)	1.021 (1.004–1.039)
Source mass	1.041 (1.018–1.064)	1.035 (1.008–1.063)	1.034 (0.986–1.083)	1.037 (0.993–1.084)
Factors	1.037 (1.015–1.059)	1.050 (1.023–1.077)	1.032 (0.988–1.077)	1.054 (1.013–1.096)
Components	1.026 (0.997–1.054)	1.029 (0.999–1.059)	1.030 (0.981–1.083)	1.033 (0.993–1.074)
Source mass + secondary aerosols	1.090 (1.058–1.122)	1.061 (1.020–1.103)	1.087 (1.023–1.155)	1.063 (1.000–1.130)
Factors + secondary aerosols	1.073 (1.045–1.102)	1.086 (1.051–1.122)	1.072 (1.019–1.127)	1.089 (1.040–1.141)
Components + secondary aerosols	1.070 (1.034–1.107)	1.029 (0.992–1.068)	1.074 (1.015–1.136)	1.041 (0.993–1.092)
45 MSAs with SO_2 Data (240,692 Subjects)				
SO_2	1.003 (0.988–1.018)	0.998 (0.976–1.020)	1.019 (0.980–1.059)	1.002 (0.972–1.033)
$PM_{2.5}$ mass	1.024 (1.013–1.035)	1.014 (0.998–1.030)	1.031 (1.001–1.061)	1.012 (0.988–1.036)
Source mass	1.087 (1.042–1.133)	0.968 (0.908–1.031)	1.121 (1.026–1.225)	0.984 (0.910–1.065)
Factors	1.039 (1.000–1.081)	1.068 (1.016–1.122)	1.075 (0.997–1.158)	1.072 (1.015–1.132)
Components	1.008 (0.952–1.068)	1.025 (0.960–1.095)	1.030 (0.960–1.104)	1.026 (0.960–1.095)
$PM_{2.5}$ mass + SO_2	1.024 (1.006–1.042)	1.007 (0.983–1.032)	1.042 (0.997–1.089)	1.009 (0.976–1.043)
Source mass + SO_2	1.095 (1.048–1.144)	0.968 (0.909–1.031)	1.132 (1.034–1.238)	0.985 (0.910–1.065)
Factors + SO_2	1.032 (0.991–1.075)	1.069 (1.015–1.125)	1.075 (0.996–1.162)	1.074 (1.015–1.137)
Components + SO_2	1.018 (0.955–1.084)	1.038 (0.968–1.113)	1.044 (0.967–1.126)	1.038 (0.968–1.114)

Table continues next page

[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.5 (*Continued*). TRIs for CVD Mortality for Combinations of $PM_{2.5}$ Mass and Sets of Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Sets of Variables in TRI Formulation	Standard Cox Model: Without Ecologic Covariates	Standard Cox Model: With Ecologic Covariates	Random Effects Cox Model: Without Ecologic Covariates	Random Effects Cox Model: With Ecologic Covariates
51 MSAs with NO_2 Data (289,522 Subjects)				
NO_2	0.999 (0.989–1.009)	1.025 (1.010–1.041)	0.991 (0.963–1.020)	1.026 (1.002–1.051)
$PM_{2.5}$ mass	1.021 (1.011–1.031)	1.019 (1.005–1.032)	1.022 (0.998–1.045)	1.014 (0.994–1.034)
Source mass	1.047 (1.008–1.087)	0.998 (0.946–1.053)	1.050 (0.978–1.126)	1.011 (0.945–1.080)
Factors	1.045 (1.008–1.082)	1.067 (1.022–1.114)	1.053 (0.993–1.117)	1.069 (1.021–1.119)
Components	1.015 (0.963–1.070)	0.981 (0.923–1.043)	1.026 (0.956–1.101)	0.981 (0.923–1.043)
$PM_{2.5}$ mass + NO_2	1.014 (1.002–1.026)	1.031 (1.014–1.048)	1.007 (0.977–1.038)	1.029 (1.003–1.055)
Source mass + NO_2	1.046 (1.007–1.086)	0.998 (0.946–1.053)	1.051 (0.982–1.126)	0.999 (0.946–1.055)
Factors + NO_2	1.042 (1.006–1.080)	1.061 (1.016–1.108)	1.049 (0.989–1.113)	1.062 (1.015–1.112)
Components + NO_2	0.995 (0.937–1.055)	0.998 (0.934–1.067)	1.009 (0.936–1.088)	0.998 (0.934–1.067)
68 MSAs with O_3 Data (343,638 Subjects)				
O_3	1.010 (1.003–1.016)	0.994 (0.986–1.003)	1.014 (1.001–1.028)	1.001 (0.986–1.017)
$PM_{2.5}$ mass	1.023 (1.013–1.033)	1.024 (1.012–1.037)	1.025 (1.003–1.047)	1.020 (1.000–1.042)
Source mass	1.053 (1.019–1.089)	1.024 (0.977–1.074)	1.072 (1.003–1.145)	1.051 (0.982–1.126)
Factors	1.055 (1.021–1.090)	1.084 (1.041–1.129)	1.074 (1.013–1.140)	1.098 (1.042–1.156)
Components	1.022 (0.977–1.069)	1.003 (0.958–1.050)	1.051 (0.981–1.126)	1.011 (0.962–1.062)
$PM_{2.5}$ mass + O_3	1.028 (1.017–1.039)	1.018 (1.004–1.032)	1.028 (1.006–1.050)	1.019 (0.996–1.042)
Source mass + O_3	1.053 (1.019–1.089)	1.031 (0.982–1.081)	1.070 (1.002–1.144)	1.052 (0.983–1.126)
Factors + O_3	1.051 (1.015–1.088)	1.079 (1.034–1.126)	1.080 (1.015–1.148)	1.096 (1.037–1.158)
Components + O_3	1.022 (0.977–1.069)	1.004 (0.959–1.052)	1.050 (0.980–1.125)	1.010 (0.961–1.060)

[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.6. TRIs for All-Cause Mortality for Combinations of $PM_{2.5}$ Mass and Sets of Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Set of Variables in TRI Formulation	Standard Cox Model: Without Ecologic Covariates	Standard Cox Model: With Ecologic Covariates	Random Effects Cox Model: Without Ecologic Covariates	Random Effects Cox Model: With Ecologic Covariates
100 MSAs (445,860 Subjects)				
$PM_{2.5}$ mass	1.006 (1.001–1.012)	1.013 (1.006–1.019)	1.013 (0.999–1.026)	1.014 (1.002–1.026)
Source mass	1.004 (0.990–1.018)	1.029 (1.012–1.047)	1.010 (0.980–1.042)	1.033 (1.002–1.064)
Factors	1.006 (0.992–1.020)	1.035 (1.018–1.053)	1.012 (0.985–1.041)	1.040 (1.011–1.070)
Components	1.022 (1.004–1.041)	1.032 (1.013–1.051)	1.025 (0.994–1.057)	1.032 (1.004–1.062)
Source mass + secondary aerosols	1.012 (0.993–1.032)	1.040 (1.014–1.066)	1.032 (0.991–1.075)	1.053 (1.009–1.099)
Factors + secondary aerosols	1.014 (0.997–1.032)	1.053 (1.031–1.075)	1.029 (0.996–1.063)	1.063 (1.027–1.100)
Components + secondary aerosols	1.043 (1.020–1.066)	1.035 (1.011–1.060)	1.043 (1.007–1.080)	1.042 (1.007–1.079)
45 MSAs with SO_2 Data (240,692 Subjects)				
SO_2	1.001 (0.991–1.010)	1.002 (0.988–1.017)	1.017 (0.990–1.045)	1.016 (0.990–1.043)
$PM_{2.5}$ mass	0.999 (0.992–1.006)	1.012 (1.001–1.022)	1.014 (0.992–1.036)	1.015 (0.994–1.038)
Source mass	1.013 (0.986–1.042)	0.994 (0.954–1.036)	1.053 (0.991–1.120)	1.022 (0.961–1.086)
Factors	1.010 (0.985–1.036)	1.052 (1.019–1.086)	1.023 (0.979–1.069)	1.062 (1.020–1.106)
Components	1.027 (0.989–1.066)	1.036 (0.993–1.082)	1.027 (0.989–1.066)	1.037 (0.993–1.082)
$PM_{2.5}$ mass + SO_2	1.000 (0.989–1.011)	1.009 (0.993–1.025)	1.027 (0.995–1.061)	1.023 (0.994–1.054)
Source mass + SO_2	1.025 (0.996–1.054)	0.995 (0.955–1.037)	1.065 (1.003–1.131)	1.024 (0.964–1.087)
Factors + SO_2	1.017 (0.990–1.044)	1.070 (1.035–1.106)	1.034 (0.989–1.080)	1.076 (1.036–1.117)
Components + SO_2	1.055 (1.013–1.100)	1.072 (1.024–1.122)	1.056 (1.013–1.100)	1.072 (1.024–1.122)

Table continues next page

[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.6 (*Continued*). TRIs for All-Cause Mortality for Combinations of $PM_{2.5}$ Mass and Sets of Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Set of Variables in TRI Formulation	Standard Cox Model: Without Ecologic Covariates	Standard Cox Model: With Ecologic Covariates	Random Effects Cox Model: Without Ecologic Covariates	Random Effects Cox Model: With Ecologic Covariates
51 MSAs with NO_2 Data (289,522 Subjects)				
NO_2	0.986 (0.980–0.993)	1.011 (1.001–1.021)	0.989 (0.969–1.010)	1.018 (0.997–1.039)
$PM_{2.5}$ mass	0.998 (0.991–1.004)	1.013 (1.004–1.021)	1.006 (0.989–1.023)	1.011 (0.995–1.028)
Source mass	0.985 (0.961–1.009)	0.994 (0.960–1.029)	1.007 (0.962–1.054)	1.010 (0.963–1.059)
Factors	1.007 (0.984–1.030)	1.043 (1.014–1.072)	1.015 (0.981–1.051)	1.045 (1.012–1.080)
Components	1.020 (0.985–1.055)	1.014 (0.974–1.055)	1.029 (0.987–1.072)	1.014 (0.974–1.055)
$PM_{2.5}$ mass + NO_2	0.989 (0.981–0.997)	1.016 (1.005–1.027)	0.995 (0.973–1.019)	1.020 (0.999–1.043)
Source mass + NO_2	0.985 (0.961–1.009)	0.994 (0.960–1.029)	1.007 (0.962–1.055)	1.011 (0.964–1.061)
Factors + NO_2	1.001 (0.978–1.024)	1.037 (1.008–1.066)	1.009 (0.977–1.042)	1.038 (1.007–1.069)
Components + NO_2	1.041 (1.002–1.082)	1.035 (0.991–1.081)	1.041 (1.002–1.082)	1.035 (0.991–1.081)
68 MSAs with O_3 Data (343,638 Subjects)				
O_3	1.001 (1.006–1.015)	1.003 (0.998–1.009)	1.008 (0.998–1.017)	1.004 (0.993–1.015)
$PM_{2.5}$ mass	0.999 (0.992–1.005)	1.012 (1.004–1.020)	1.008 (0.993–1.023)	1.013 (0.998–1.028)
Source mass	0.988 (0.967–1.009)	1.015 (0.984–1.046)	1.018 (0.973–1.065)	1.043 (0.991–1.098)
Factors	1.002 (0.981–1.024)	1.041 (1.014–1.069)	1.029 (0.989–1.071)	1.067 (1.023–1.112)
Components	1.017 (0.987–1.047)	1.007 (0.978–1.038)	1.031 (0.988–1.077)	1.017 (0.980–1.057)
$PM_{2.5}$ mass + O_3	1.007 (1.000–1.014)	1.013 (1.004–1.022)	1.010 (0.995–1.025)	1.014 (0.997–1.030)
Source mass + O_3	0.987 (0.967–1.009)	1.011 (0.980–1.043)	1.016 (0.972–1.062)	1.040 (0.988–1.093)
Factors + O_3	1.007 (0.985–1.030)	1.051 (1.022–1.081)	1.031 (0.990–1.075)	1.075 (1.029–1.122)
Components + O_3	1.018 (0.988–1.048)	1.005 (0.976–1.036)	1.031 (0.988–1.077)	1.016 (0.978–1.055)

[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.7. TRIs for Cardiopulmonary Mortality for Combinations of $PM_{2.5}$ Mass and Sets of Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Set of Variables in TRI Formulation	Standard Cox Model: Without Ecologic Covariates	Standard Cox Model: With Ecologic Covariates	Random Effects Cox Model: Without Ecologic Covariates	Random Effects Cox Model: With Ecologic Covariates
100 MSAs (445,860 Subjects)				
$PM_{2.5}$ mass	1.030 (1.022–1.038)	1.032 (1.023–1.042)	1.031 (1.012–1.050)	1.027 (1.010–1.043)
Source mass	1.020 (1.000–1.041)	1.025 (1.001–1.051)	1.017 (0.974–1.063)	1.027 (0.985–1.071)
Factors	1.027 (1.008–1.047)	1.049 (1.024–1.074)	1.025 (0.985–1.066)	1.050 (1.012–1.090)
Components	1.027 (1.001–1.053)	1.034 (1.007–1.062)	1.031 (0.985–1.080)	1.035 (0.996–1.075)
Source mass + secondary aerosols	1.074 (1.046–1.104)	1.074 (1.037–1.113)	1.080 (1.021–1.141)	1.077 (1.017–1.141)
Factors + secondary aerosols	1.057 (1.032–1.083)	1.083 (1.051–1.116)	1.061 (1.014–1.110)	1.088 (1.040–1.137)
Components + secondary aerosols	1.068 (1.036–1.102)	1.037 (1.003–1.072)	1.071 (1.018–1.128)	1.049 (1.002–1.098)
45 MSAs with SO_2 Data (240,692 Subjects)				
SO_2	0.990 (0.977–1.004)	0.998 (0.977–1.018)	1.012 (0.976–1.048)	1.005 (0.975–1.035)
$PM_{2.5}$ mass	1.022 (1.013–1.032)	1.022 (1.007–1.036)	1.033 (1.006–1.060)	1.020 (0.997–1.044)
Source mass	1.068 (1.028–1.110)	0.996 (0.941–1.055)	1.102 (1.020–1.190)	1.016 (0.942–1.096)
Factors	1.027 (0.991–1.064)	1.064 (1.018–1.113)	1.054 (0.991–1.122)	1.073 (1.017–1.133)
Components	1.014 (0.963–1.069)	1.029 (0.969–1.092)	1.034 (0.969–1.103)	1.029 (0.969–1.092)
$PM_{2.5}$ mass + SO_2	1.010 (0.994–1.026)	1.011 (0.989–1.034)	1.037 (0.996–1.079)	1.016 (0.984–1.050)
Source mass + SO_2	1.082 (1.040–1.126)	0.998 (0.942–1.057)	1.116 (1.034–1.205)	1.017 (0.944–1.096)
Factors + SO_2	1.026 (0.989–1.065)	1.072 (1.023–1.124)	1.061 (0.994–1.132)	1.083 (1.024–1.145)
Components + SO_2	1.030 (0.973–1.091)	1.051 (0.986–1.120)	1.054 (0.983–1.130)	1.051 (0.986–1.120)

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[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.7 (*Continued*). TRIs for Cardiopulmonary Mortality for Combinations of $PM_{2.5}$ Mass, Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Set of Variables in TRI Formulation	Standard Cox Model: Without Ecologic Covariates	Standard Cox Model: With Ecologic Covariates	Random Effects Cox Model: Without Ecologic Covariates	Random Effects Cox Model: With Ecologic Covariates
51 MSAs with NO_2 Data (289,522 Subjects)				
NO_2	1.000 (0.991–1.009)	1.024 (1.010–1.038)	0.996 (0.969–1.023)	1.026 (1.003–1.051)
$PM_{2.5}$ mass	1.021 (1.012–1.030)	1.026 (1.014–1.038)	1.025 (1.004–1.047)	1.022 (1.004–1.041)
Source mass	1.030 (0.995–1.066)	1.021 (0.972–1.072)	1.036 (0.974–1.101)	1.031 (0.970–1.096)
Factors	1.029 (0.997–1.063)	1.062 (1.021–1.104)	1.037 (0.988–1.089)	1.065 (1.020–1.113)
Components	1.020 (0.973–1.071)	1.000 (0.945–1.057)	1.033 (0.971–1.098)	1.000 (0.946–1.057)
$PM_{2.5}$ mass + NO_2	1.015 (1.004–1.026)	1.035 (1.019–1.050)	1.013 (0.985–1.042)	1.033 (1.009–1.058)
Source mass + NO_2	1.029 (0.994–1.065)	1.021 (0.972–1.072)	1.037 (0.977–1.101)	1.021 (0.972–1.073)
Factors + NO_2	1.026 (0.994–1.060)	1.057 (1.016–1.099)	1.034 (0.984–1.086)	1.060 (1.014–1.107)
Components + NO_2	1.011 (0.958–1.067)	1.018 (0.958–1.082)	1.024 (0.958–1.095)	1.018 (0.958–1.082)
68 MSAs with O_3 Data (343,638 Subjects)				
O_3	1.014 (1.008–1.020)	0.998 (0.991–1.005)	1.018 (1.005–1.030)	1.005 (0.991–1.019)
$PM_{2.5}$ mass	1.023 (1.014–1.032)	1.030 (1.018–1.041)	1.028 (1.008–1.048)	1.027 (1.008–1.046)
Source mass	1.036 (1.006–1.067)	1.041 (0.997–1.087)	1.054 (0.995–1.116)	1.061 (0.997–1.130)
Factors	1.037 (1.007–1.068)	1.075 (1.036–1.116)	1.055 (1.004–1.108)	1.085 (1.038–1.135)
Components	1.024 (0.983–1.066)	1.007 (0.966–1.050)	1.046 (0.985–1.111)	1.015 (0.969–1.063)
$PM_{2.5}$ mass + O_3	1.031 (1.021–1.041)	1.025 (1.013–1.038)	1.032 (1.012–1.052)	1.026 (1.006–1.047)
Source mass + O_3	1.036 (1.006–1.067)	1.045 (1.001–1.092)	1.052 (0.994–1.114)	1.062 (0.998–1.131)
Factors + O_3	1.033 (1.001–1.066)	1.071 (1.030–1.114)	1.056 (1.003–1.112)	1.084 (1.033–1.136)
Components + O_3	1.025 (0.984–1.068)	1.008 (0.967–1.052)	1.046 (0.985–1.111)	1.015 (0.969–1.063)

[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.8. TRIs for Lung Cancer Mortality for Combinations of $PM_{2.5}$ Mass and Sets of Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Sets of Variables in TRI Formulation	Standard Cox Model: Without Ecologic Covariates	Standard Cox Model: With Ecologic Covariates	Random Effects Cox Model: Without Ecologic Covariates	Random Effects Cox Model: With Ecologic Covariates
100 MSAs (445,860 Subjects)				
$PM_{2.5}$ mass	1.019 (0.998–1.041)	1.019 (0.995–1.043)	1.021 (0.996–1.048)	1.019 (0.995–1.043)
Source mass	1.010 (0.958–1.065)	1.013 (0.949–1.081)	1.010 (0.957–1.065)	1.013 (0.949–1.081)
Factors	0.962 (0.915–1.013)	0.963 (0.904–1.026)	0.961 (0.911–1.015)	0.963 (0.904–1.026)
Components	0.946 (0.884–1.011)	0.947 (0.882–1.016)	0.945 (0.883–1.013)	0.947 (0.882–1.016)
Source mass + secondary aerosols	1.083 (1.007–1.165)	1.083 (1.007–1.165)	1.083 (1.007–1.165)	1.083 (1.007–1.165)
Factors + secondary aerosols	1.028 (0.964–1.097)	1.026 (0.948–1.110)	1.028 (0.964–1.097)	1.026 (0.948–1.110)
Components + secondary aerosols	1.045 (0.962–1.135)	1.018 (0.932–1.113)	1.045 (0.962–1.135)	1.018 (0.932–1.113)
45 MSAs with SO_2 Data (240,692 Subjects)				
SO_2	1.009 (0.973–1.046)	0.993 (0.941–1.048)	1.011 (0.965–1.058)	0.993 (0.941–1.048)
$PM_{2.5}$ mass	1.016 (0.990–1.044)	1.020 (0.981–1.060)	1.021 (0.987–1.056)	1.020 (0.981–1.060)
Source mass	1.121 (1.011–1.244)	1.067 (0.912–1.248)	1.121 (1.011–1.244)	1.067 (0.912–1.248)
Factors	1.042 (0.948–1.145)	1.063 (0.946–1.194)	1.042 (0.948–1.145)	1.063 (0.946–1.195)
Components	1.178 (1.027–1.351)	1.189 (1.014–1.395)	1.178 (1.027–1.351)	1.189 (1.014–1.395)
$PM_{2.5}$ mass + SO_2	1.023 (0.980–1.068)	1.007 (0.950–1.067)	1.027 (0.975–1.083)	1.007 (0.950–1.067)
Source mass + SO_2	1.121 (1.006–1.250)	1.064 (0.910–1.245)	1.121 (1.006–1.250)	1.064 (0.910–1.245)
Factors + SO_2	1.060 (0.961–1.169)	1.102 (0.975–1.246)	1.060 (0.961–1.169)	1.102 (0.975–1.246)
Components + SO_2	1.217 (1.047–1.415)	1.239 (1.045–1.468)	1.217 (1.047–1.415)	1.239 (1.045–1.468)

Table continues next page

[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.8 (*Continued*). TRIs for Lung Cancer Mortality for Combinations of $PM_{2.5}$ Mass and Sets of Source Mass, Factors, Secondary Aerosols, and Components with Individual Gases Added[a]

Sets of Variables in TRI Formulation	Standard Cox Model: Without Ecologic Covariates	Standard Cox Model: With Ecologic Covariates	Random Effects Cox Model: Without Ecologic Covariates	Random Effects Cox Model: With Ecologic Covariates
51 MSAs with NO_2 Data (289,522 Subjects)				
NO_2	0.971 (0.947–0.996)	0.976 (0.940–1.013)	0.971 (0.947–0.996)	0.976 (0.940–1.013)
$PM_{2.5}$ mass	1.012 (0.996–1.047)	1.025 (0.993–1.058)	1.023 (0.997–1.050)	1.025 (0.993–1.058)
Source mass	1.116 (1.016–1.226)	1.114 (0.974–1.274)	1.116 (1.016–1.226)	1.114 (0.974–1.274)
Factors	1.035 (0.949–1.128)	1.028 (0.928–1.139)	1.035 (0.949–1.128)	1.028 (0.928–1.139)
Components	1.071 (0.943–1.216)	1.039 (0.895–1.208)	1.071 (0.943–1.216)	1.039 (0.895–1.208)
$PM_{2.5}$ mass + NO_2	0.995 (0.966–1.024)	0.995 (0.956–1.036)	0.995 (0.966–1.024)	0.995 (0.956–1.036)
Source mass + NO_2	1.116 (1.016–1.225)	1.114 (0.974–1.273)	1.116 (1.016–1.225)	1.114 (0.974–1.273)
Factors + NO_2	1.035 (0.948–1.130)	1.027 (0.926–1.140)	1.035 (0.948–1.130)	1.027 (0.926–1.140)
Components + NO_2	1.035 (0.895–1.196)	1.032 (0.875–1.217)	1.035 (0.895–1.196)	1.032 (0.875–1.217)
68 MSAs with O_3 Data (343,638 Subjects)				
O_3	1.014 (0.998–1.030)	1.007 (0.987–1.028)	1.013 (0.996–1.030)	1.007 (0.987–1.028)
$PM_{2.5}$ mass	1.016 (0.993–1.041)	1.016 (0.986–1.046)	1.019 (0.992–1.047)	1.016 (0.986–1.046)
Source mass	1.072 (0.989–1.163)	1.057 (0.943–1.184)	1.072 (0.989–1.163)	1.057 (0.943–1.184)
Factors	0.993 (0.916–1.077)	0.984 (0.892–1.086)	0.993 (0.916–1.077)	0.984 (0.892–1.086)
Components	1.017 (0.913–1.132)	1.008 (0.903–1.124)	1.017 (0.913–1.132)	1.008 (0.903–1.124)
$PM_{2.5}$ mass + O_3	1.024 (0.998–1.051)	1.019 (0.987–1.053)	1.025 (0.997–1.053)	1.019 (0.987–1.053)
Source mass + O_3	1.072 (0.988–1.162)	1.050 (0.937–1.178)	1.072 (0.988–1.162)	1.050 (0.937–1.178)
Factors + O_3	0.987 (0.906–1.075)	0.977 (0.881–1.083)	0.987 (0.906–1.075)	0.977 (0.881–1.083)
Components + O_3	1.020 (0.915–1.136)	1.011 (0.905–1.129)	1.020 (0.915–1.136)	1.011 (0.905–1.129)

[a] Data are presented by analytic model (standard Cox or random effects Cox) with or without ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race. Values show increase in risk per increase in exposure equal to the magnitude of the IQR (95% CIs). IQRs were calculated on the full data sets: 100 MSAs with CPS-II subjects in residence (full dataset for mortality analyses); 45 MSAs with SO_2 data; 51 MSAs with local NO_2 data; and 68 MSAs with O_3 data.

Table I.9. Model Fit Statistics for CVD and IHD Mortality Models Including Sets of Factors and NO_2[a]

TRI Formulation		Number of MSAs and Subjects	Standard Cox Model				Random Effects Cox Model			
			Wald Test *df* *P* Value	NO_2 Tercile[b]			Wald Test *df* *P* Value	NO_2 Tercile[b]		
1	2			1	2	3		1	2	3
CVD Mortality										
$PM_{2.5}$ mass	NO_2 + NO_2–factor interactions	51 289,522	5.5357 1 0.0186	0.9237	0.9022	0.9166	1.6839 1 0.1944	0.9492	0.9370	0.9490
Factors	NO_2 + NO_2–factor interactions	51 289,522	11.7505 8 0.1627	1.0389	1.0546	1.0535	8.4934 8 0.3868	1.0106	1.0446	1.0757
Factors + secondary aerosols	NO_2 + NO_2–factor interactions	51 289,522	22.1499 11 0.0232	1.0616	1.1004	1.1204	22.1275 11 0.0234	1.0107	1.0447	1.0759
Factors (no Metals)	NO_2 + NO_2–factor interactions	46 261,279	16.4431 7 0.0214	1.0318	1.0981	1.1550	15.9038 7 0.0260	1.0319	1.0985	1.1566
Factors (no Metals) + secondary aerosols	NO_2 + NO_2–factor interactions	46 261,279	29.9658 10 0.0009	1.0725	1.1688	1.2488	29.1473 10 0.0009	1.0724	1.1687	1.2488
IHD Mortality										
$PM_{2.5}$ mass	NO_2 + NO_2–factor interactions	51 289,522	2.1748 1 0.1403	0.9555	0.9529	0.9660	0.8727 1 0.3502	0.9475	0.9391	0.9556
Factors	NO_2 + NO_2–factor interactions	51 289,522	22.2464 8 0.0045	0.8994	0.9705	1.1102	10.1746 8 0.2530	0.9388	1.0504	1.2478
Factors + secondary aerosols	NO_2 + NO_2–factor interactions	51 289,522	52.5383 11 0.0001	0.9162	1.0845	1.3862	39.4216 11 0.0001	0.9349	1.0828	1.3420
Factors (no Metals)	NO_2 + NO_2–factor interactions	46 261,279	12.6069 7 0.0823	1.0062	1.1337	1.2847	9.7409 7 0.2037	0.9989	1.1431	1.3426
Factors (no Metals) + secondary aerosols	NO_2 + NO_2–factor interactions	46 261,279	60.6090 10 0.0001	1.2030	1.5011	1.7800	60.5562 10 0.0001	1.2029	1.5010	1.7800

[a] Data are presented by analytic model (standard Cox or random effects Cox) with ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race.

[b] TRI estimates were evaluated at the terciles of NO_2: tercile 1 at 10.6 ppb; tercile 2 at 15.7 ppb; and tercile 3 at 23.6 ppb.

Table I.10. Pearson Correlations for NO_2 with Individual Components, Factors, and Secondary Aerosols

Components and Secondary Aerosols	
As	−0.1582
Ca	0.3151
Cu	0.7282
Cl	0.3215
Fe	0.7567
Pb	0.1889
Mn	0.4461
Ni	0.3910
Se	−0.1802
V	0.6559
Si	0.2349
Zn	0.3728
K	0.1791
Na	0.4803
Mg	0.3661
EC	0.8171
SO_4^{2-}	−0.2620
OC	0.5423
NO_3^-	0.6185
$PM_{2.5}$	0.4497
Factors and Secondary Aerosols[a]	
Soil	0.1789
Metals	−0.2922
Traffic	0.9150
Salt	0.4047
Residual oil combustion	0.5500
Steel	0.4223
Coal combustion	−0.2974
Biomass combustion	0.1208
SO_4^{2-}	−0.2682
OC	0.5494
NO_3^-	0.6243

[a] Factors and secondary aerosols were evaluated at the MSA level.

Table I.11. Standard Deviation and Ratio of 3rd to 1st Quartile of the Subject-Level Distribution of the TRIs for CVD and IHD Mortality[a]

TRI Formulation	Number of MSAs and Subjects	Standard Cox Model		Random Effects Cox Model	
		Standard Deviation	Ratio 3rd/1st Quartile	Standard Deviation	Ratio 3rd/1st Quartile
CVD Mortality					
$PM_{2.5}$ mass	51 289,522	0.020	1.020 (1.006–1.035)	0.014	1.015 (1.001–1.037)
Factors	51 289,522	0.039	1.043 (1.026–1.071)	0.044	1.058 (1.027–1.107)
Factors + secondary aerosols	51 289,522	0.049	1.065 (1.039–1.100)	0.048	1.064 (1.037–1.105)
Factors (no Metals)	46 261,279	0.040	1.058 (1.032–1.095)	0.046	1.070 (1.036–1.113)
Factors (no Metals) + secondary aerosols	46 261,279	0.037	1.061 (1.037–1.095)	0.037	1.059 (1.036–1.094)
IHD Mortality					
$PM_{2.5}$ mass	51 289,522	0.013	1.014 (1.001–1.033)	0.024	1.024 (1.001–1.061)
Factors	51 289,522	0.050	1.063 (1.036–1.102)	0.058	1.091 (1.045–1.164)
Factors + secondary aerosols	51 289,522	0.065	1.084 (1.050–1.141)	0.066	1.100 (1.053–1.178)
Factors (no Metals)	46 261,279	0.061	1.091 (1.058–1.143)	0.072	1.108 (1.052–1.192)
Factors (no Metals) + secondary aerosols	46 261,279	0.076	1.117 (1.071–1.178)	0.076	1.111 (1.060–1.190)

[a] Data are presented by analytic model (standard Cox or random effects Cox) with ecologic covariates for subsets of MSAs. Models were adjusted for 42 individual-level covariates, stratifying the baseline hazard function by age (1-year groupings), gender, and race.

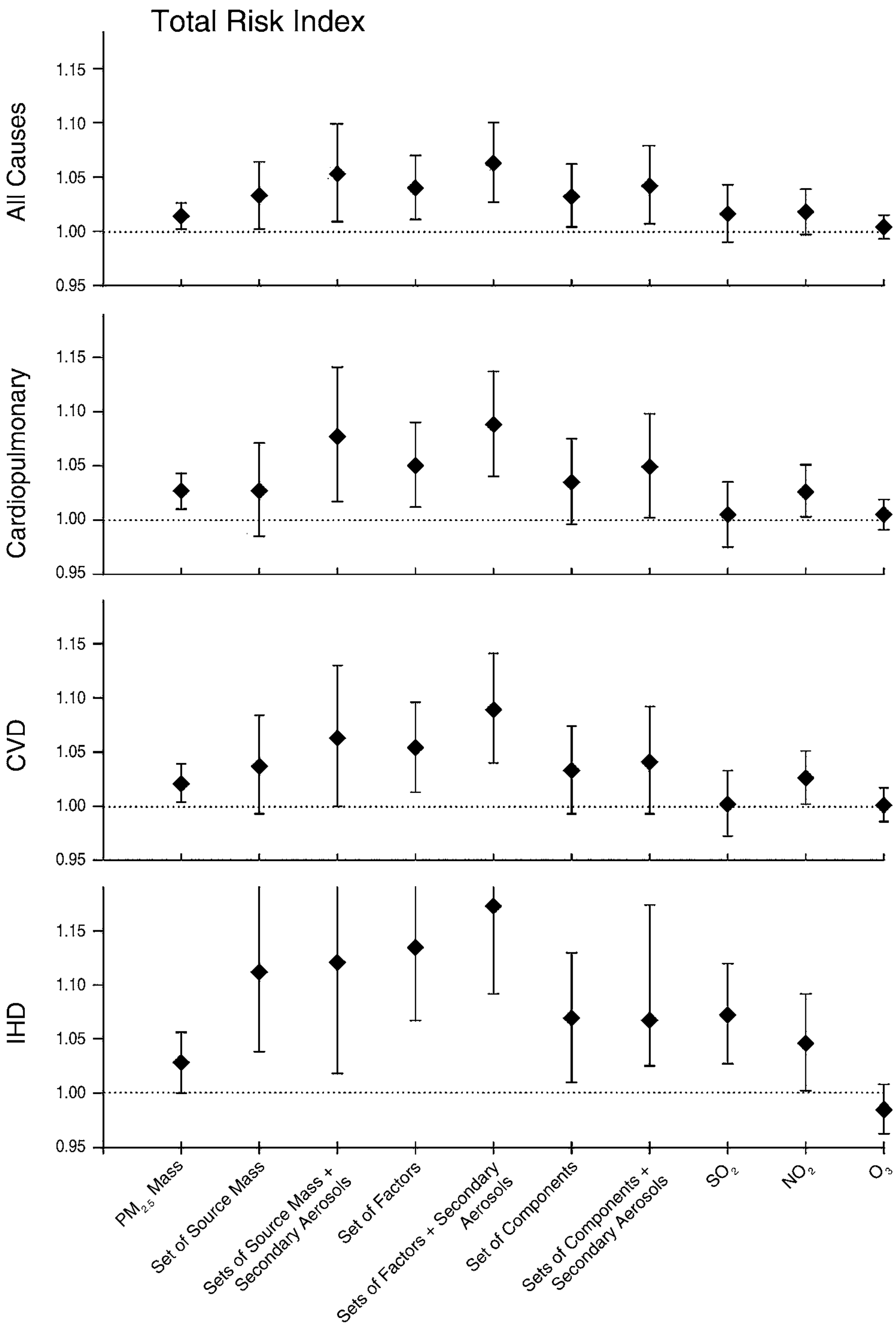

Figure I.1. TRIs (with 95% CIs) at the IQR from the random effects Cox model including individual-level and ecologic covariates.