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Part 2

Association of Daily Mortality with Ambient Air Pollution, and Effect Modification by Extremely High Temperature in Wuhan, China

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with a Commentary by the HEI Health Review Committee

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INVESTIGATORS' REPORT

Part 2. Association of Daily Mortality with Ambient Air Pollution, and Effect Modification by Extremely High Temperature in Wuhan, China

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ABSTRACT

Fewer studies have been published on the association between daily mortality and ambient air pollution in Asia than in the United States and Europe. This study was undertaken in Wuhan, China, to investigate the acute effects of air pollution on mortality with an emphasis on particulate matter (PM*). There were three primary aims: (1) to examine the associations of daily mortality due to all natural causes and daily cause-specific mortality (cardiovascular [CVD], stroke, cardiac [CARD], respiratory [RD], cardiopulmonary [CP], and non-cardiopulmonary [non-CP] causes) with daily mean concentrations ($\mu g/m^3$) of PM with an aerodynamic diameter $\leq$ 10 μm (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), or ozone (O_3); (2) to investigate the effect modification of extremely high temperature on the association between air pollution and daily mortality due to all natural causes and daily cause-specific mortality; and (3) to assess the uncertainty of effect estimates caused by the change in International Classification of Disease (ICD) coding of mortality data from Revision 9 (ICD-9) to Revision 10 (ICD-10) code.

Wuhan is called an "oven city" in China because of its extremely hot summers (the average daily temperature in July is 37.2°C and maximum daily temperature often exceeds 40°C). Approximately 4.5 million residents live in the core city area of 201 km^2, where air pollution levels are higher and ranges are wider than the levels in most cities studied in the published literature.

We obtained daily mean levels of PM_{10}, SO_2, and NO_2 concentrations from five fixed-site air monitoring stations operated by the Wuhan Environmental Monitoring Center (WEMC). O_3 data were obtained from two stations, and 8-hour averages, from 10:00 to 18:00, were used. Daily mortality data were obtained from the Wuhan Centres for Disease Prevention and Control (WCDC) during the study period of July 1, 2000, to June 30, 2004.

To achieve the first aim, we used a regression of the logarithm of daily counts of mortality due to all natural causes and cause-specific mortality on the daily mean concentrations of the four pollutants while controlling for weather, temporal factors, and other important covariates with generalized additive models (GAMs). We derived pollutant effect estimations for 0-day, 1-day, 2-day, 3-day, and 4-day lagged exposure levels, and the averages of 0-day and 1-day lags (lag 0–1 day) and of 0-day, 1-day, 2-day, and 3-day lags (lag 0–3 days) before the event of death. In addition, we used individual-level data (e.g., age and sex) to classify subgroups in stratified analyses. Furthermore, we explored the nonlinear shapes ("thresholds") of the exposure–response relations.

To achieve the second aim, we tested the hypothesis that extremely high temperature modifies the associations between air pollution and daily mortality. We developed three corresponding weather indicators: "extremely hot,"

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The PAPA Program was initiated by the Health Effects Institute in part to support the Clean Air Initiative for Asian Cities (CAI-Asia), a partnership of the Asian Development Bank and the World Bank to inform regional decisions about improving air quality in Asia. Additional funding was obtained from the U.S. Agency for International Development and the William and Flora Hewlett Foundation. The contents of this document have not been reviewed by private party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views or policies of these parties, and no endorsement by them should be inferred.

*A list of abbreviations and other terms appears at the end of the Investigators' Report.

"extremely cold," and "normal temperatures." The estimates were obtained from the models for the main effects and for the pollutant–temperature interaction for each pollutant and each cause of mortality.

To achieve the third aim, we conducted an additional analysis. We examined the concordance rates and kappa statistics between the ICD-9-coded mortality data and the ICD-10-coded mortality data for the year 2002. We also compared the magnitudes of the estimated effects resulting from the use of the two types of ICD-coded mortality data.

In general, the largest pollutant effects were observed at lag 0–1 day. Therefore, for this report, we focused on the results obtained from the lag 0–1 models. We observed consistent associations between PM_{10} and mortality: every 10-μg/m^3 increase in PM_{10} daily concentration at lag 0–1 day produced a statistically significant association with an increase in mortality due to all natural causes (0.43%; 95% confidence interval [CI], 0.24 to 0.62), CVD (0.57%; 95% CI, 0.31 to 0.84), stroke (0.57%; 95% CI, 0.25 to 0.88), CARD (0.49%; 95% CI, 0.04 to 0.94), RD (0.87%; 95% CI, 0.34 to 1.41), CP (0.52%; 95% CI, 0.27 to 0.77), and non-CP (0.30%; 95% CI, 0.05 to 0.54). In general, these effects were stronger in females than in males and were also stronger among the elderly (≥ 65 years) than among the young.

The results of sensitivity testing over the range of exposures from 24.8 to 477.8 μg/m^3 also suggest the appropriateness of assuming a linear relation between daily mortality and PM_{10}. Among the gaseous pollutants, we also observed statistically significant associations of mortality with NO_2 and SO_2, and that the estimated effects of these two pollutants were stronger than the PM_{10} effects. The patterns of NO_2 and SO_2 associations were similar to those of PM_{10} in terms of sex, age, and linearity. O_3 was not associated with mortality.

In the analysis of the effect modification of extremely high temperature on the association between air pollution and daily mortality, only the interaction of PM_{10} with temperature was statistically significant. Specifically, the interaction terms were statistically significant for mortality due to all natural ($P = 0.014$), CVD ($P = 0.007$), and CP ($P = 0.014$) causes. Across the three temperature groups, the strongest PM_{10} effects occurred mainly on days with extremely high temperatures for mortality due to all natural (2.20%; 95% CI, 0.74 to 3.68), CVD (3.28%; 95% CI, 1.24 to 5.37), and CP (3.02%; 95% CI, 1.03 to 5.04) causes. The weakest effects occurred at normal temperature days, with the effects on days with low temperatures in the middle.

To assess the uncertainty of the effect estimates caused by the change from ICD-9-coded mortality data to ICD-10-coded mortality data, we compared the two sets of data and found high concordance rates (> 99.3%) and kappa statistics close to 1.0 (> 0.98). All effect estimates showed very little change. All statistically significant levels of the estimated effects remained unchanged.

In conclusion, the findings for the aims from the current study are consistent with those in most previous studies of air pollution and mortality. The small differences between mortality effects for deaths coded using ICD-9 and ICD-10 show that the change in coding had a minimal impact on our study. Few published papers have reported synergistic effects of extremely high temperatures and air pollution on mortality, and further studies are needed. Establishing causal links between heat, PM_{10}, and mortality will require further toxicologic and cohort studies.

INTRODUCTION

Ambient air pollution has been associated with a wide range of effects on human health, including measurable decrements in lung function (Pope et al. 1991; Frampton et al. 1995; Seaton et al. 1995; Peters et al. 1999) and increases in respiratory symptoms and diseases (Lebowitz et al. 1987; Pope et al. 1995; Pikhart et al. 2000), hospital and emergency department admissions (Bates et al. 1990; Thurston et al. 1992), and mortality (Dockery et al. 1993; Zmirou et al. 1996; Goldberg et al. 2000, 2003; Dominici et al. 2002b; Schwartz 2003). A large number of daily mortality time-series analyses have provided sufficiently convincing evidence that mortality due to all natural causes, including CP, is associated with ambient PM exposure in the United States (Zmirou et al. 1998; Dominici et al. 2002a), Canada (Burnett et al. 2000; Goldberg et al. 2000, 2003), Eastern Germany (Spix et al. 1993), China (Xu et al. 1994, 2000), Korea (Lee et al. 2000), Greece (Katsouyanni et al. 1993), and Brazil (Saldiva et al. 1994). The estimated effect of PM_{10} in previous studies has generally been cited as a 0.42% increase in mortality due to all natural causes for a 10-μg/m^3 change in daily PM_{10} at lag 0–1 day (Goldberg et al. 2000, 2003; Ostro et al. 2006).

Despite the large body of available evidence, the establishment of PM exposure as a cause of increased mortality is still elusive because of several uncertainties: (1) the mortality rates attributed to PM exposure are not specific and may also be attributable to other factors such as exposure to copollutants, a change in climate, or personal and sociodemographic factors affecting PM exposure (e.g., the use of air conditioners and level of education); (2) the evidence indicating the general shape of the exposure–response curve showing the relations between PM and mortality is insufficient; (3) PM mortality effect estimates are heterogeneous; (4) models are misspecified; and (5) plausible biologic mechanisms that explain the observed associations have

yet to be demonstrated. In addition, studies conducted in Asia have been limited compared with the number of studies in North America and Europe (Lee et al. 2000; Wong et al. 2001; Wong et al. 2002). Also, results of published Asian studies have been called into question for probable imprecision in the PM effect estimates, which were derived from analyses based on smaller data sets of available air pollution data (e.g., data based only on total suspended particles for PM) or of fewer deaths (e.g., only one year's mortality data) in some cities (Xu et al. 1994, 2000). Nevertheless, the results from these published Asian studies show a consistent association between ambient levels of PM pollution and daily mortality.

SPECIFIC AIMS

Our long-term goal is to determine the health effects of exposure to high levels of outdoor and indoor air pollution on the residents living in Wuhan, China. The overall objective of this project was to examine associations between daily mortality counts and daily mean concentrations of PM_{10}. The central hypothesis was that daily ambient PM_{10} concentrations are associated with daily mortality due to all natural causes, as well as cause-specific mortality. We tested our central hypothesis and achieved the overall objective of this study by pursuing the following three specific aims:

1. To examine associations of daily mortality due to all natural causes and daily cause-specific mortality with daily mean concentrations of PM_{10}, SO_2, NO_2, or O_3, using analyses based on the Protocol for Coordinated Time-Series Studies of Daily Mortality in Asian Cities (called in this report the "Common Protocol," found at the end of this volume).
2. To determine the effect modification of extremely high temperatures on the association between air pollution and daily mortality.
3. To assess the uncertainty of effect estimates due to the change from ICD-9-coded mortality data to ICD-10-coded mortality data.

METHODS AND STUDY DESIGN

This study was conducted to determine whether daily variations in ambient PM_{10} concentrations in Wuhan during the four-year period from July 1, 2000, to June 30, 2004, were associated with daily variations in mortality due to all natural causes and in cause-specific mortality. Several important and unique aspects relevant to the study design are worth mentioning. First, there are approximately 4.5 million people residing in the nine urban core districts of Wuhan covering 201 km^2, and this high-density population has been stable since early 1990. Second, historically there have been high concentrations of ambient $PM_{2.5}$, $PM_{10-2.5}$, PM_{10}, and gaseous pollutants SO_2 and NO_2, with concentration ranges wider than ranges reported in the published literature (Waldman et al. 1991; Qian et al. 2001). Third, extremely high temperatures occur every summer, and air conditioners are seldom used. Last, it has already been demonstrated that there is a statistically significant difference in respiratory symptoms and diseases among children and adults, and in lung function among children living in the urban core districts compared with those living in the suburban districts of Wuhan (Waldman et al. 1991; He et al. 1993; Qian et al. 2000, 2001). By selecting all permanent residents living in the nine core urban districts, we reduced or minimized misclassification of the study population's exposure.

STUDY AREA

Wuhan is the capital of Hubei Province, which is located in the middle of the Yangzi River delta, at latitude 29°58′ to 31°22′ N and longitude 113°41′ to 115°05′ E (Figure 1). Its population is approximately 7.5 million, and approximately 4.5 million people reside in nine core urban districts within an area of 201 km^2. Wuhan has a subtropical, humid monsoon climate with hot and humid summers. Its average daily temperature in July is 37.2°C, and the maximum daily temperature often exceeds 40°C. Because of its hot summers, Wuhan has been called an "oven city" in China. The major industries in Wuhan include ferrous smelters and chemical, power, and machinery plants. Wuhan is one of the biggest hubs for land, water, and air transportation in China. The major sources of air pollution in the city are motor vehicles and coal used for domestic cooking, heating, and industrial processes. With high daily mean PM_{10} concentrations, a wide PM_{10} concentration range, and low and high temperature fluctuations over a

Figure 1. Map of China showing the location of the city of Wuhan.

long period of time, Wuhan provides a unique opportunity to examine the effect of the combination of ambient air pollution and extremely high temperature on daily mortality using a large mortality data set (Qian et al. 2001).

DATA SOURCES

All the data came from three sources (Table 1). Mortality data were obtained from the WCDC. Pollution data were collected in the substations of the Wuhan Air Automatic Monitoring System (WAAMS), which is operated by the WEMC. WAAMS fixed-site air monitoring stations have been measuring daily mean concentrations of PM_{10}, SO_2, NO_2, and O_3 since 2000. Weather data were routinely collected at the Wuhan Meteorological Station, which is operated by the Wuhan Meteorological Administration (WMA).

Air Pollution Data

Fixed-site air monitoring stations of WAAMS, which were operated by WEMC and certified by the U.S. Environmental Protection Agency (U.S. EPA), provided daily mean ambient concentrations of PM_{10}, SO_2, and NO_2 for the period of July 1, 2000, to June 30, 2004 (Figure 2 and Table 2). These measurements were collected automatically and continuously, 24 hours per day and 365 days per year. The monitoring stations were located at Jiangan (station 1), Hanyang (station 2), Nanzhan (station 3), Wugang (station 4), Donghu (station 5), Jiantan (station 6), and Kifa (station 7). Eight-hour (measured from 10:00–18:00) mean concentrations of O_3 during the same time period were provided by two of the monitoring stations (one O_3 monitor was located at station 5, and the other was located at station 6, but was then moved to station 7 during the time period of the study).

All pollutant measurements followed standardized methods (Table 2). PM_{10} measurements were made using PM_{10} beta-attenuation mass monitors (Dasibi Environmental Corporation Model 7001); SO_2 measurements were made using an ultraviolet fluorescence analyzer (Dasibi Environmental Corporation Model 4108); NO_2 measurements were made using a chemiluminescence analyzer (Dasibi Environmental Corporation Model 2108); and O_3 measurements were made using an ultraviolet photometry analyzer (Dasibi Environmental Corporation Model 1008). The operation of the WAAMS by the WEMC strictly followed the quality assurance/quality control procedure set by the State Environmental Protection Administration of China (SEPA 1992) (see Appendix I; available on the HEI Web site). Briefly, the WEMC conducts regularly scheduled performance audits and precision checks on the air monitoring equipment. Quarterly performance audits are conducted of the PM_{10}, SO_2, NO_2, and O_3 monitoring systems to assess data accuracy. We calculated a surrogate exposure variable for a participant's daily exposure using a simple averaging method.

Mortality Data

All mortality data, collected between July 1, 2000, and June 30, 2004, were obtained from the computerized database of the WCDC. The data were collected daily and covered all permanent residents of the nine core urban districts of Wuhan. Mortality data had been collected according to the Standard Operating Procedure for Mortality Data Collection in Wuhan (Appendix J; available on the HEI Web site). In the event of a death in Wuhan, the government requires that the decedent's family obtain a death certificate from a hospital or a local community clinic to remove the deceased person's name from the government-controlled household registration. The decedent's family must then submit the death certificate to both the local police station and local public health station in order to obtain a cremation certificate.

Per regulatory policy, the WCDC electronically archives all death certificates. In 1992, the WCDC was the first center in China to standardize its system for the collection of mortality data. This system, which was approved and recommended by the Chinese Department of Health, requires (1) that mortality data be validated four times a

Table 1. Summary of Original Data Sets

Data Set	Source	Description of Contents
Mortality	Wuhan Centres for Disease Prevention and Control (WCDC)	Death certificates, including name, birth date, sex, date and place of death, education levels, occupation, and underlying cause of death (ICD-9- or ICD-10-coded).
Pollutants	Wuhan Environmental Monitoring Center (WEMC)	PM_{10}, SO_2, and NO_2 (daily mean concentrations); O_3 (8-hour mean concentrations)
Weather	Wuhan Meteorological Administration (WMA)	Daily average air temperature and daily average relative humidity

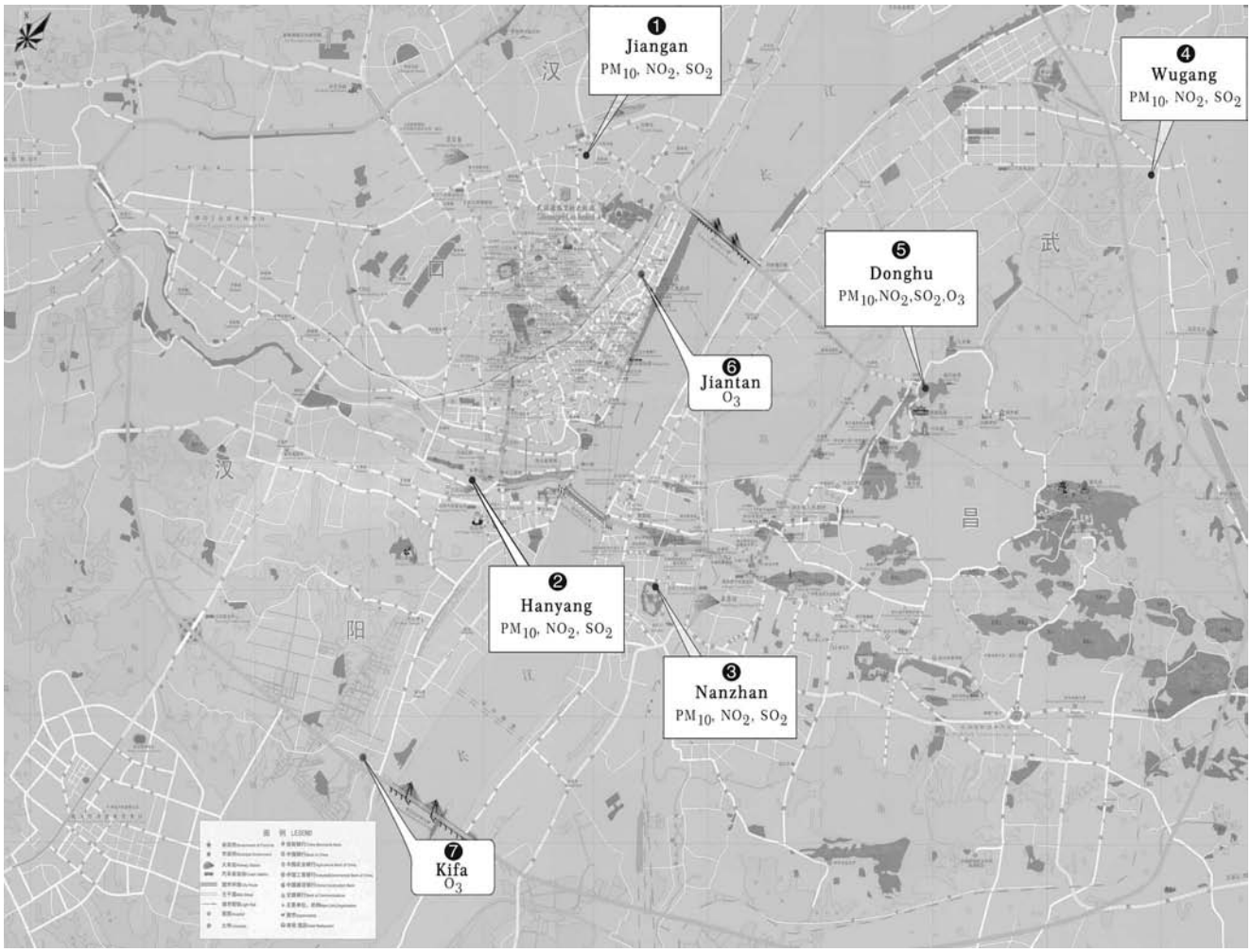


Figure 2. Map of Wuhan showing ambient air monitoring stations. Stations 1, 2, 3, and 4 monitored PM_{10}, NO_2, and SO_2. Stations 6 and 7 monitored O_3 only and took measurements sequentially (the monitor was moved from one station to the other during the monitoring period). Station 5 monitored all four criteria pollutants.

Table 2. Summary of Particulate Matter and Gaseous Pollutant Data Available for the Present Study, July 1, 2000, to June 30, 2004

Pollutant	Start Year	Number of Sites	Duration	Frequency	Samplers Used	Analytic Methods
PM_{10}	2000	5	Hourly	Continuous	Dasibi 7001	Automated beta-attenuation mass sampler
NO_2	2000	5	Hourly	Continuous	Dasibi 2108	Chemiluminescence
SO_2	2000	5	Hourly	Continuous	Dasibi 4108	Ultraviolet fluorescence
O_3	2000	2	Hourly	Continuous	Dasibi 1008	UV photometry

year; (2) that death events collected from the WCDC conform with those collected from the Wuhan Police Department; (3) that no missing data exist on any death certificates; (4) that undetermined causes of death compose less than 2% of recorded deaths in urban districts; and (5) that a correct coding rate of greater than 98% be achieved for cause-specific deaths. Identifying information, such as age, sex, date of death, place of death, residence at time of death, occupation, education level, and the underlying cause of death noted in either ICD-9 or ICD-10 code, is recorded on the death certificate. The date of the change from ICD-9 to ICD-10 coding was January 1, 2003.

Total mortality was divided into the following underlying causes of death in this study:

- All natural mortality (ICD-9: 1–799; ICD-10: A00–R99)
- Cardiovascular diseases (CVD) (ICD-9: 390–459; ICD-10: I00–I99)
- Cerebrovascular diseases, or stroke (ICD-9: 430–438; ICD-10: I60–I69)
- Cardiac, or heart diseases (CARD) (ICD-9: 390–398, 410–429; ICD-10: I00–I09, I20–I52)
- Respiratory diseases (RD) (ICD-9: 460–519; ICD-10: J00–J98)
- Cardiopulmonary diseases (CP = RD + CVD)
- Non-cardiopulmonary natural mortality (non-CP)

Meteorologic Data

The Wuhan Meteorological Station is located in the Dongxihu District in the western part of Wuhan and belongs to a branch station of the global weather system in China. Meteorologic data were collected for daily average temperature and daily relative humidity (RH) from the WMA.

Combining Data from Different Sources

We abstracted ambient air pollution data from the WEMC database and merged them with the WCDC mortality data. After careful examination of potential outliers, we performed time-series analyses on these combined data to examine associations of daily variations in the concentrations of pollutants with daily variations in mortality due to all natural causes and in cause-specific mortality. After performing power calculations, we came to the conclusion that this data set has enough variation in daily exposure levels to enable us to perform time-series data analyses; that the large available population provides enough statistical power to enable us to examine the associations at different subpopulation levels (i.e., people aged $\geq$ 65 years); and that unique weather conditions and living habits provide an opportunity to test any existing confounding and/or modifying effects, such as extreme temperature on the effect estimates of the pollution–mortality relations. All statistical associations between the daily concentrations of pollutants and daily mortality were controlled for by well-known potential confounders/covariates, such as seasonal and subseasonal fluctuations in mortality, non–Poisson dispersion, weather variables, and types of gaseous pollutants.

DATA ASSURANCE PROCEDURES

Data quality assurance for the retrieved existing mortality data and air pollution data was achieved through the following efforts:

- We developed a written research protocol for this study, which included research objectives, strategies, and methods. This protocol was reviewed and approved by the HEI International Scientific Oversight Committee (ISOC).
- We documented all standard operating procedures (SOPs) for data collection (see Appendices I and J, available on the HEI Web site). For both existing mortality data and ambient air pollution data, we used only those data collected by qualified personnel and subjected to quality control procedures for further data processing and statistical analyses. The SOPs were detailed enough to be followed by individuals in a stepwise manner through the sampling, analysis, and data processing phases. In addition, the SOPs were consistent with sound scientific principles and the instrument manufacturer's specific instructions available in their respective manuals.
- We chose a relatively wide range of categories of cause of death for this study in order to reduce potential misclassification of the underlying causes of death. The rationale of this approach is that the coding process is complicated by the difficulties of determining one underlying cause of death in a complex chain of health conditions and that the accuracy of coding may vary with the cause of death among the different types of hospitals/community clinics, especially when decedents had more than one condition that concurrently contributed to death (Lauer et al. 1999; Goldberg et al. 2000; Anderson et al. 2001; Richardson 2006).
- Furthermore, we paid special attention to the recognition and identification of any potential shift in the mortality data around the time period when the ICD coding was changed from ICD-9 to ICD-10. The choice of ICD-9 or ICD-10 coding is the decision of the WCDC, and the investigators in this study had no control over it; we used whatever was available from the WCDC. Nevertheless, an additional study was conducted specifically to assess the uncertainty of effect estimates due to the ICD coding change.

- For ambient air pollution data, we used all measurements of PM_{10}, SO_2, NO_2, and O_3 concentrations collected from the available monitoring stations (only two stations were available to record O_3 concentrations) as surrogates for ambient air pollution exposure for the study population in Wuhan. We required that each monitor provide data for at least 75% of the days in a year; that at least 75% of the one-hour values of each day's measurements be available for calculating the PM_{10}, SO_2, and NO_2 24-hour average concentrations; and that at least six hourly concentrations of O_3 per day be available for calculating the 8-hour average concentrations of O_3. Our results show that very few measurements were missing or obviously erroneous. Therefore, we performed the model analysis using valid air pollution data, without having to impute missing data.
- All computerized air pollution data from the WEMC and computerized mortality data from the WCDC were sent to the Wuhan Academy of Environmental Science (WAES), where the data were stored in Excel format. The WAES was responsible for sending the data set to the Health Evaluation Sciences (HES) department of the Pennsylvania State University for verification. Descriptive analyses were conducted to obtain the frequency distributions and/or univariate distributions for the important categorical and continuous variables. The distributions for the miscoded, missing, and out-of-range data were carefully checked at HES. Errors, questions, and concerns regarding specific data points were discussed and resolved through communication with the key investigators in this study. Identical electronic copies of the finalized clean analytic database in SAS format have been stored at both the WAES and HES for subsequent data processing and analysis. Appendix H shows the audit information.

STATISTICAL METHODS AND DATA ANALYSIS

The statistical and data analysis methods are detailed in Appendix A and are based on the PAPA Common Protocol (see Protocol for Coordinated Time-Series Studies of Daily Mortality in Asian Cities, found at the end of this volume). The analytic strategies are also briefly described in this section.

We generated descriptive statistics to check the validity of the variables and to identify potential outliers. We used quasi–Poisson regression as the modeling technique in this study. Under the assumption that daily death counts follow a Poisson variate distribution with constant over- or underdispersion, we used quasi-likelihood estimation within the context of the generalized additive model (GAM) to model the natural logarithm of the expected daily death counts as a function of the predictor variables. This method accounts for the overdispersion in CIs and *P* values (Zeger and Qaqish 1988; Hastie and Tibshirani 1990). All model analyses were performed employing natural splines using the statistical software package R, version 2.5.0, with mgcv, version 1.3-24 (R Development Core Team 2007, Vienna, Austria). Appendix A presents the explicit codes used in the main statistical model. Also included are other technical details of the main regression model, including degrees of freedom per year used for the smoothing of time and the value of the overdispersion parameter.

The GAM analyses covered three major areas. First, we controlled for potential confounding of yearly, seasonal, and subseasonal variations, assuming that these variations in the mortality time series represent unmeasured processes that may confound the association between mortality and air pollution. Furthermore, visual inspection of the mortality time series showed that death counts were significantly higher over two periods: July 28 to August 3, 2003 (sum03), and December 1 to December 31, 2003 (win03). We created a three-level factor variable to indicate the two periods of high mortality and the remaining period. We controlled for the time effects by including in the base model this factor variable, which smoothed terms for the overall period as well as the three local periods.

Second, we controlled for potential confounding of relevant weather variables by using both (1) indicator variables for extremely hot days, cold days, and humid days; and (2) natural splines for the same-day (lag 0 day) temperature and RH. The extremely hot and cold days were defined as those days whose daily average temperatures were above and below the 95th and 5th percentiles of four years' worth of data, respectively (Dockery et al. 1992). The purpose of these two steps was to ensure conservative estimates of the pollution–mortality associations that we were investigating.

Finally, we regressed the effects of the air pollution variables on daily mortality (see Appendix A for the regression equation and description).

SELECTION OF THE MODEL

We built and fit the model in two steps: (1) by developing the best base model (without a pollutant) and (2) by developing the best main model (with a pollutant). The details of the model construction are presented in Appendix A.

A summary of the best base models are listed in Table 3. The residual plots of daily mortality against time after fitting the best base models are shown in Figure 3, observed and predicted deaths are shown in Figure 4, and the partial autocorrelation function (PACF) residuals plots are shown in Appendix B.

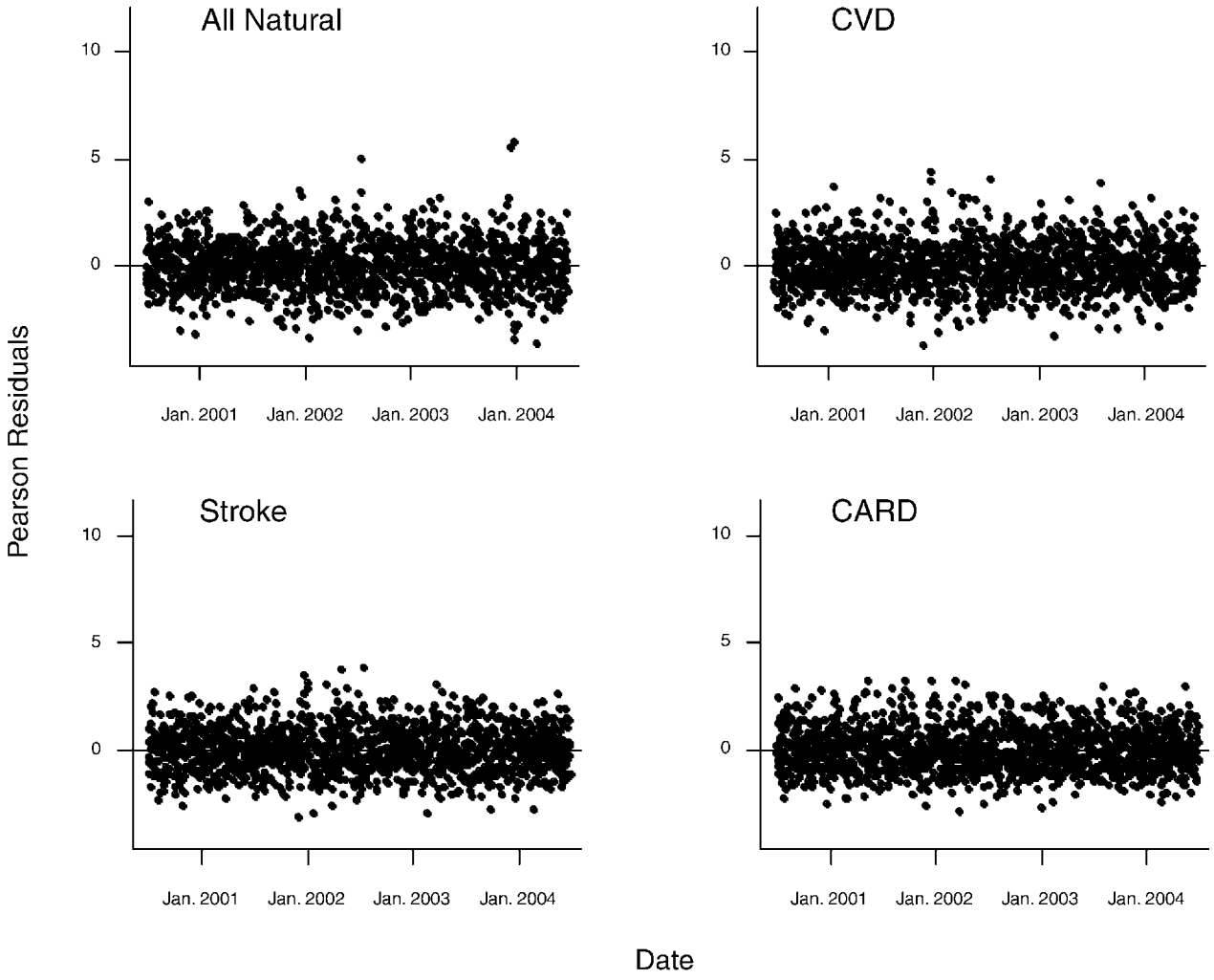


Figure 3. Pearson residual plots of daily mortality by cause of death over time.

Table 3. Summary of the Cause-Specific Mortality Base Models, July 1, 2000, to June 30, 2004[a,b]

Cause of Death	Sequential Model	Alternate Sequential Model	F1	F2	Penalized Spline Model	Best Base Model
All natural	(6,2,3,4,3)	(6,2,3,2,2)	(6,2,3,3,3)	(8,2,3,4,4)	(7,2,3,2,2)	(6,2,3,4,3)
Cardiovascular	(4,2,3,2,3)	(4,2,3,2,2)	(6,2,3,3,3)	(8,2,3,4,4)	(7,2,2,2,2)	(4,2,3,2,3)
Respiratory	(6,2,3,3,2)	(4,2,3,4,4)	(6,2,3,3,3)	(8,2,3,4,4)	(6,2,3,2,3)	(6,2,3,3,2)
Cardiac	(4,2,3,2,2)	(5,2,3,2,2)	(6,2,3,3,3)	(8,2,3,4,4)	(6,2,2,2,2)	(4,2,3,2,2)
Stroke	(4,2,3,4,4)	(4,2,3,4,4)	(6,2,3,3,3)	(8,2,3,4,4)	(6,2,2,2,2)	(4,2,3,4,4)
Cardiopulmonary	(4,2,3,3,2)	(4,2,3,2,4)	(6,2,3,3,3)	(8,2,3,4,4)	(7,3,3,2,2)	(8,2,3,4,4)
Non-cardiopulmonary	(5,2,3,3,2)	(4,2,3,2,4)	(6,2,3,3,3)	(8,2,3,4,4)	(7,2,2,2,2)	(5,2,3,3,2)

[a] The numerals in parentheses (*a*,*b*,*c*,*d*,*e*) indicate effective degrees of freedom (edf) as follows: "*a*" indicates edf per year for the time smoothing function; "*b*" indicates edf for the July 28, 2003–August 8, 2003 local time smoothing function; "*c*" indicates edf for the December 1, 2003–December 31, 2003 local time smoothing function; "*d*" indicates edf for the entire study period for the temperature smoothing function; and "*e*" indicates edf for the entire study period for the RH smoothing function.

[b] F1 and F2 indicate natural spline fixed models 1 and 2, respectively, with fixed degrees of freedom.

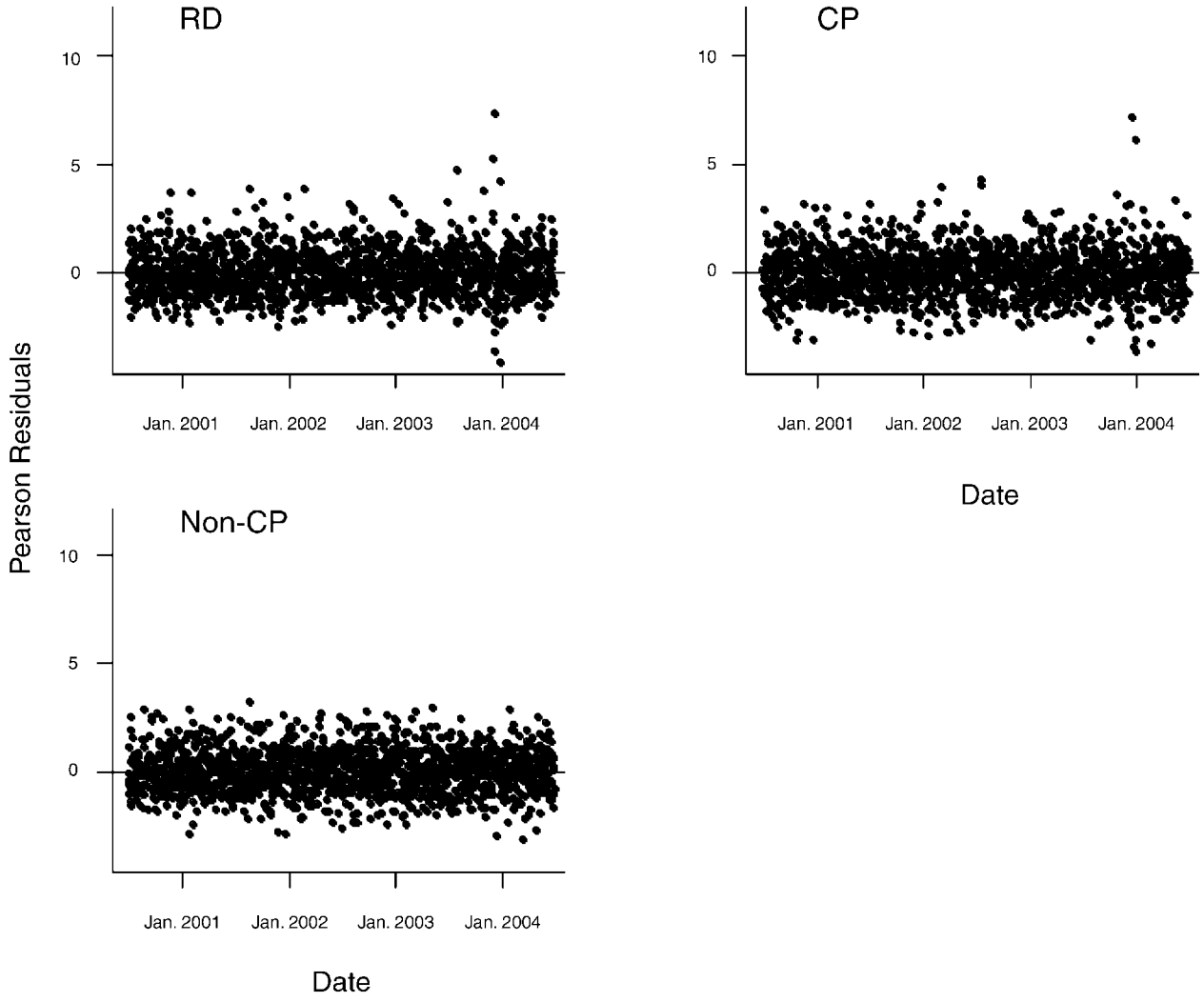


Figure 3 (*Continued*).

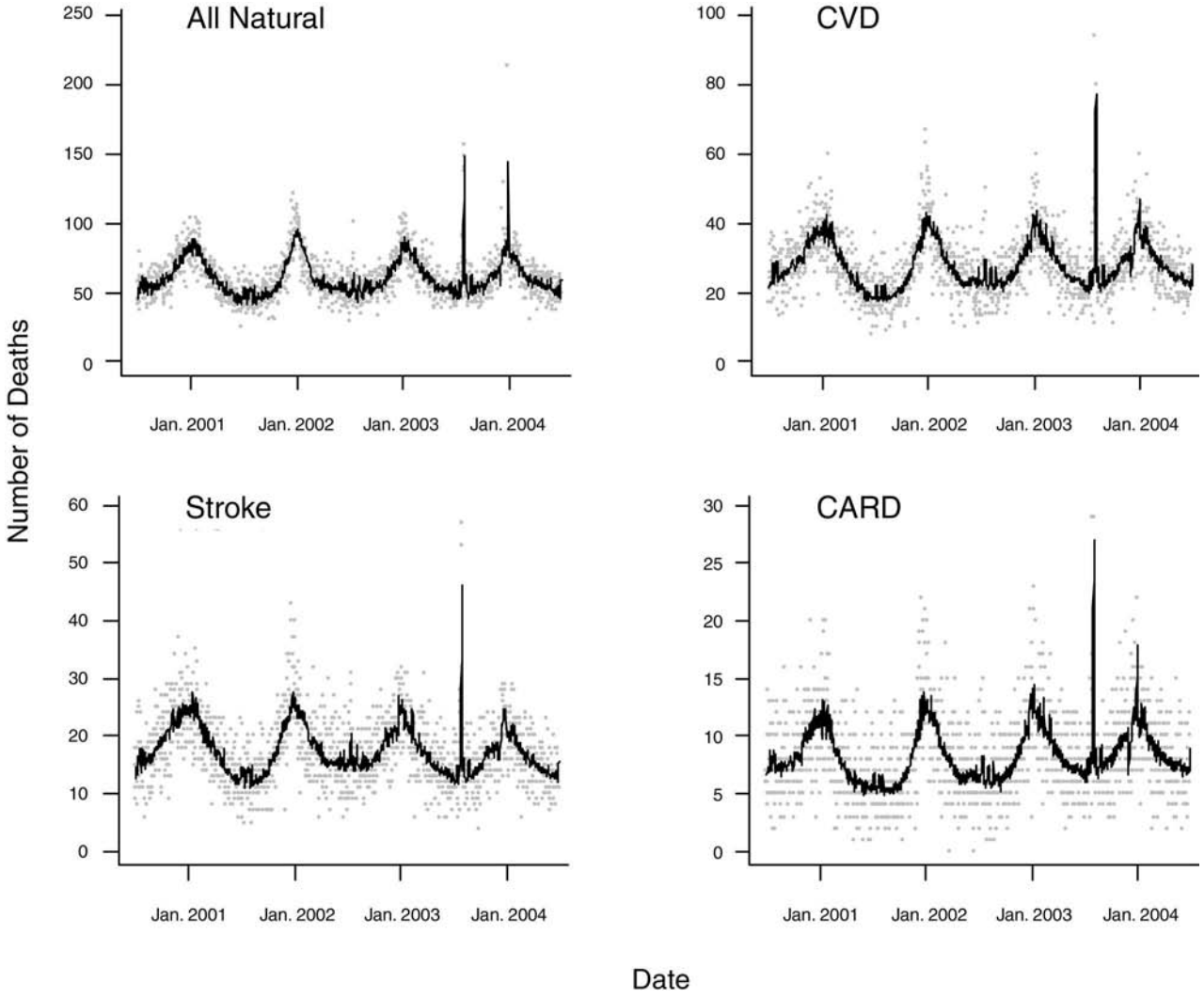


Figure 4A. Plots of observed (solid line) and predicted (lighter dots) cause-specific deaths for PM_{10} using the best main model at lag 0–1 day mean.

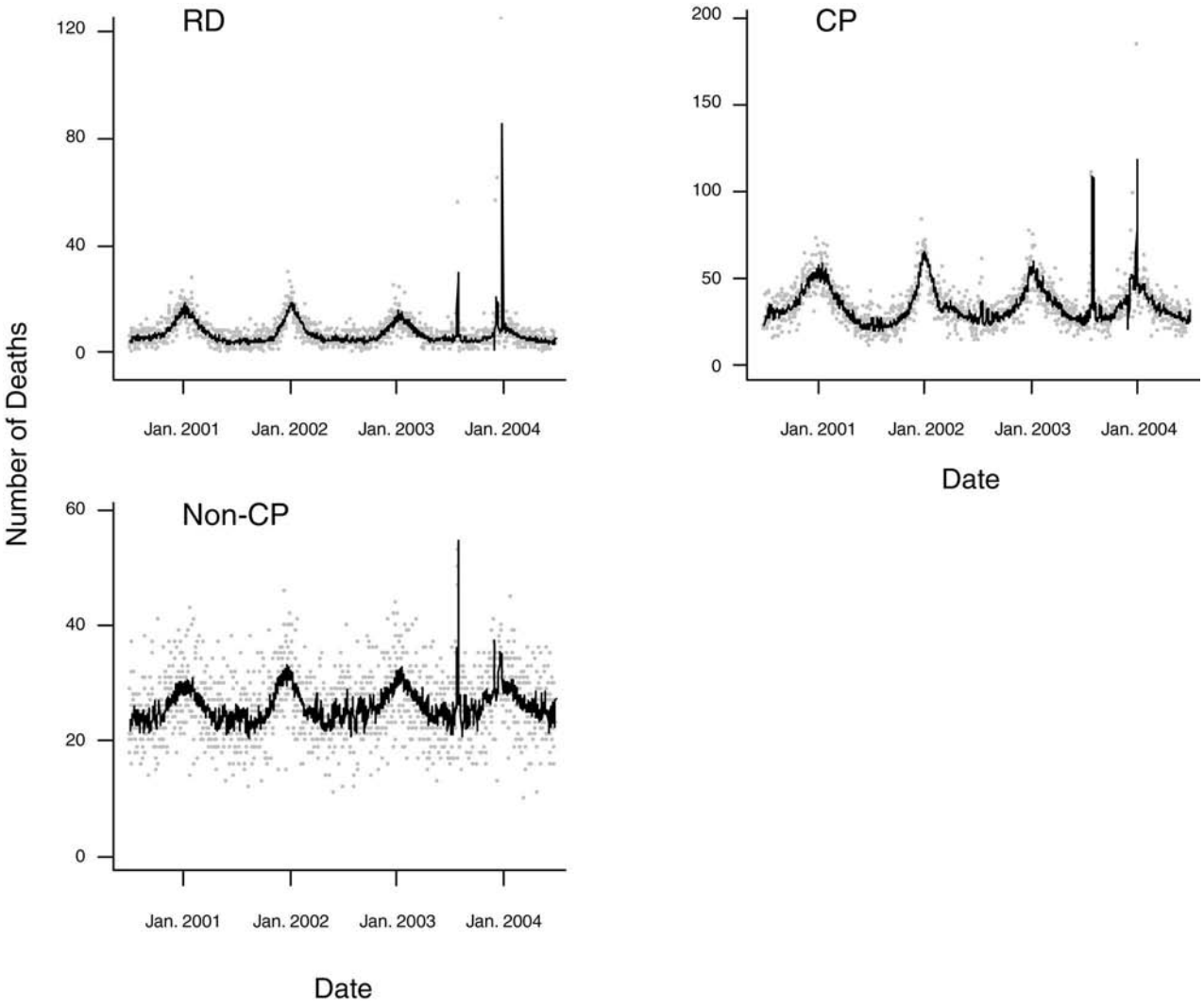


Figure 4A (*Continued*).

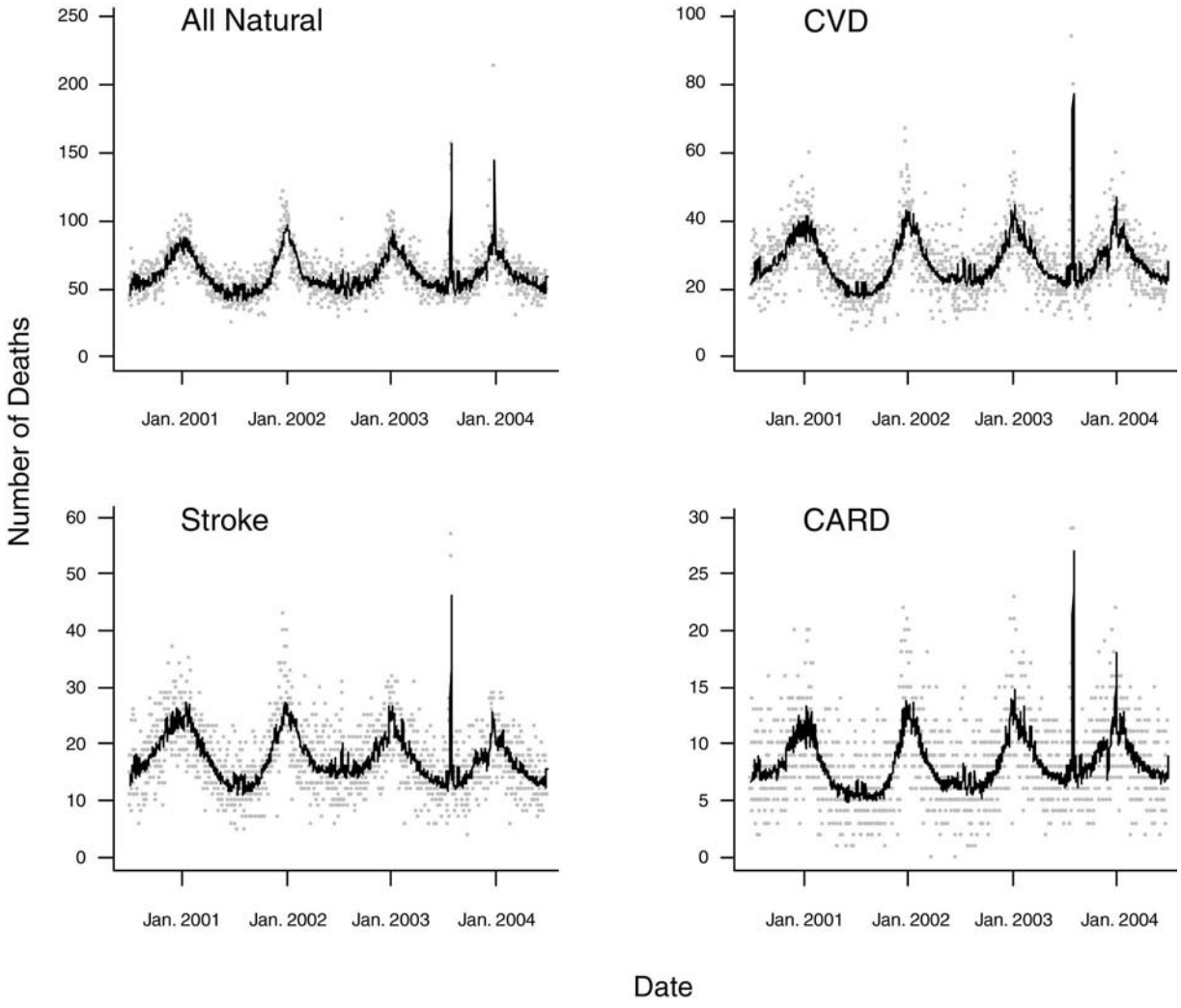


Figure 4B. Plots of observed (solid line) and predicted (lighter dots) cause-specific deaths for NO_2 using the best main model at lag 0–1 day mean.

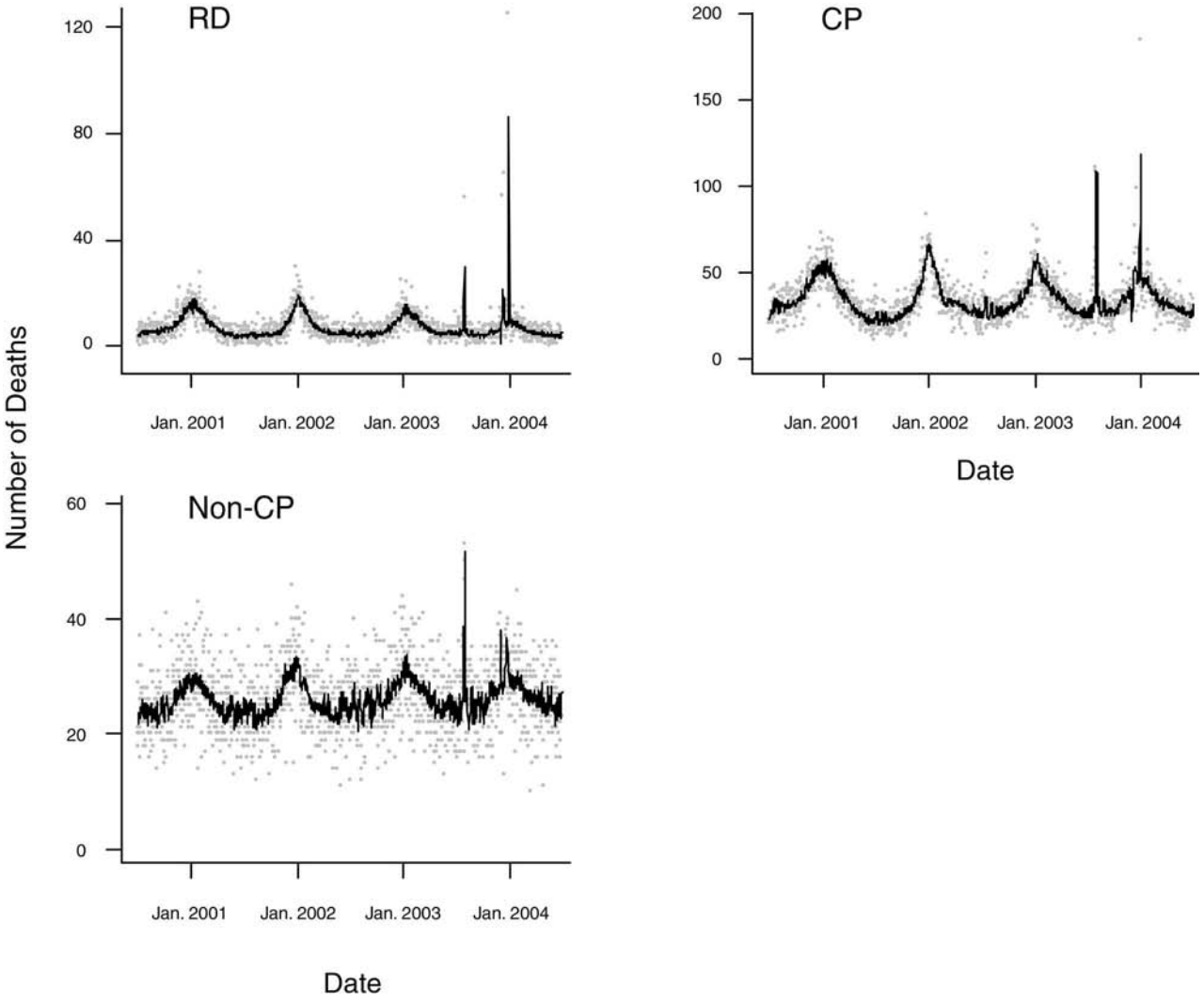


Figure 4B (*Continued*).

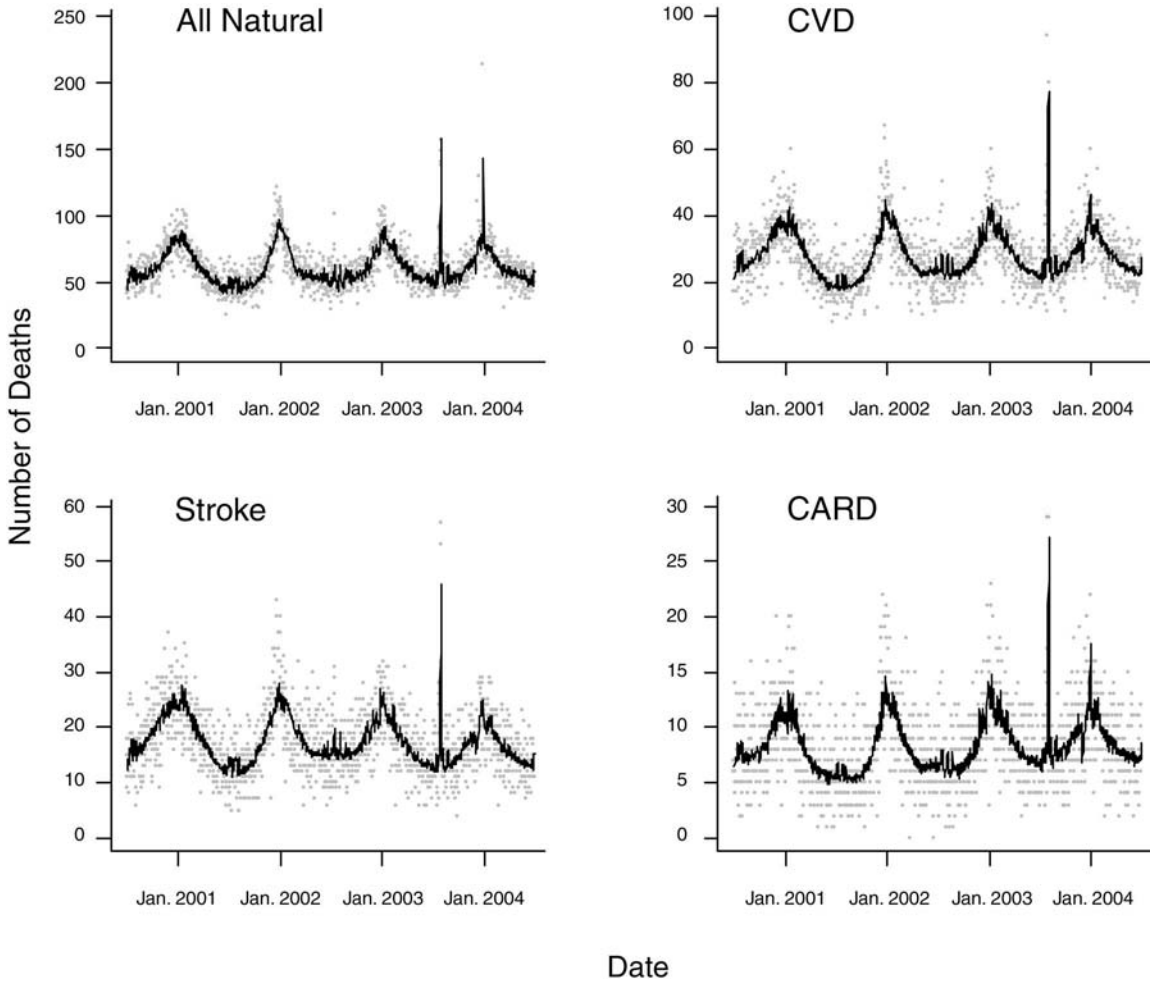


Figure 4C. Plots of observed (solid line) and predicted (lighter dots) cause-specific deaths for SO_2 using the best main model at lag 0–1 day mean.

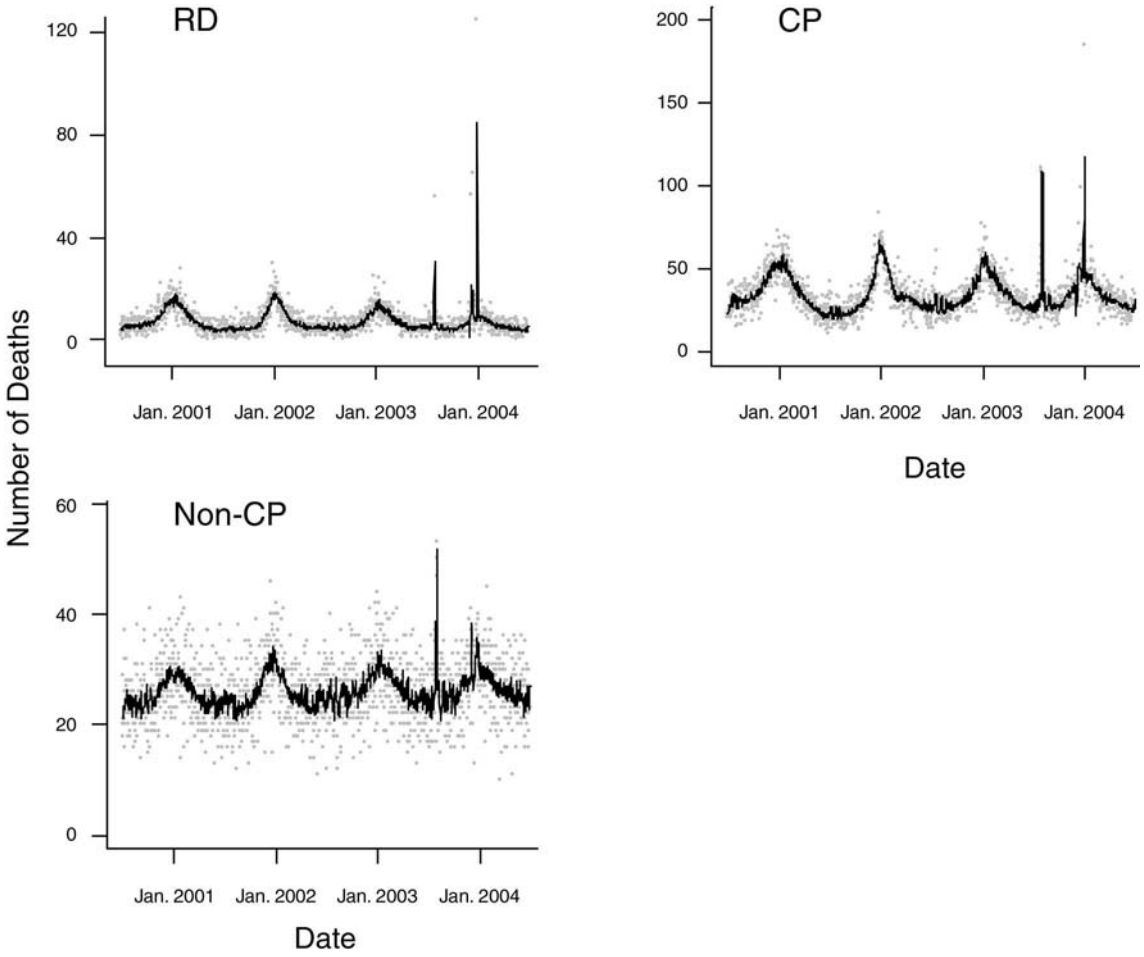


Figure 4C (*Continued*).

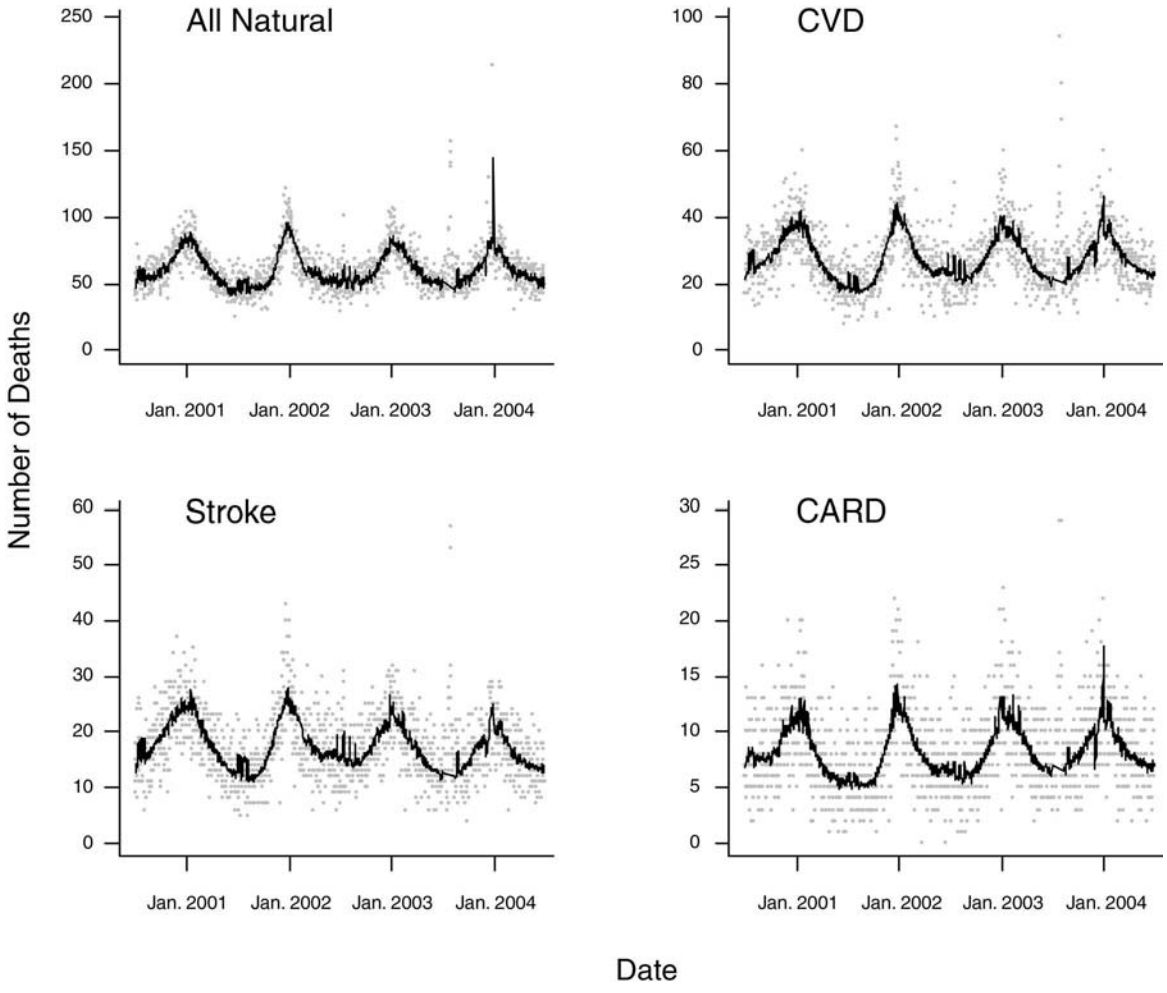


Figure 4D. Plots of observed (solid line) and predicted (lighter dots) cause-specific deaths for O_3 using the best main model at lag 0–1 day mean.

EXPOSURE–RESPONSE CURVES

Exploring exposure–response relations between daily mortality and daily mean pollutant concentrations was one of the key aims of this study. Several approaches were taken to investigate the validity of the linearity assumption for PM_{10} (the assumption that the risk associated with a given increase in exposure is the same at all levels of exposure) in the regression equation described in Appendix A. First, we plotted the exposure–response curves for the pollutant concentrations and the logarithm of the mortality counts from the fitted GAM (see Appendix A for details). Second, in the regression equation (see Appendix A), we added a quadratic term and tested its statistical significance. Last, we performed piecewise regression models by allowing different slopes of pollutant concentrations taken before and after a cutoff point (see Appendix A for details).

EXTREME WEATHER EFFECTS

Temperature variability has been shown to be an important modifier of the association between short-term ambient air pollution and mortality (Braga et al. 2002). We tested the hypothesis that extreme weather (i.e., both extremely hot and extremely cold temperatures) modifies the associations between pollution concentration and mortality.

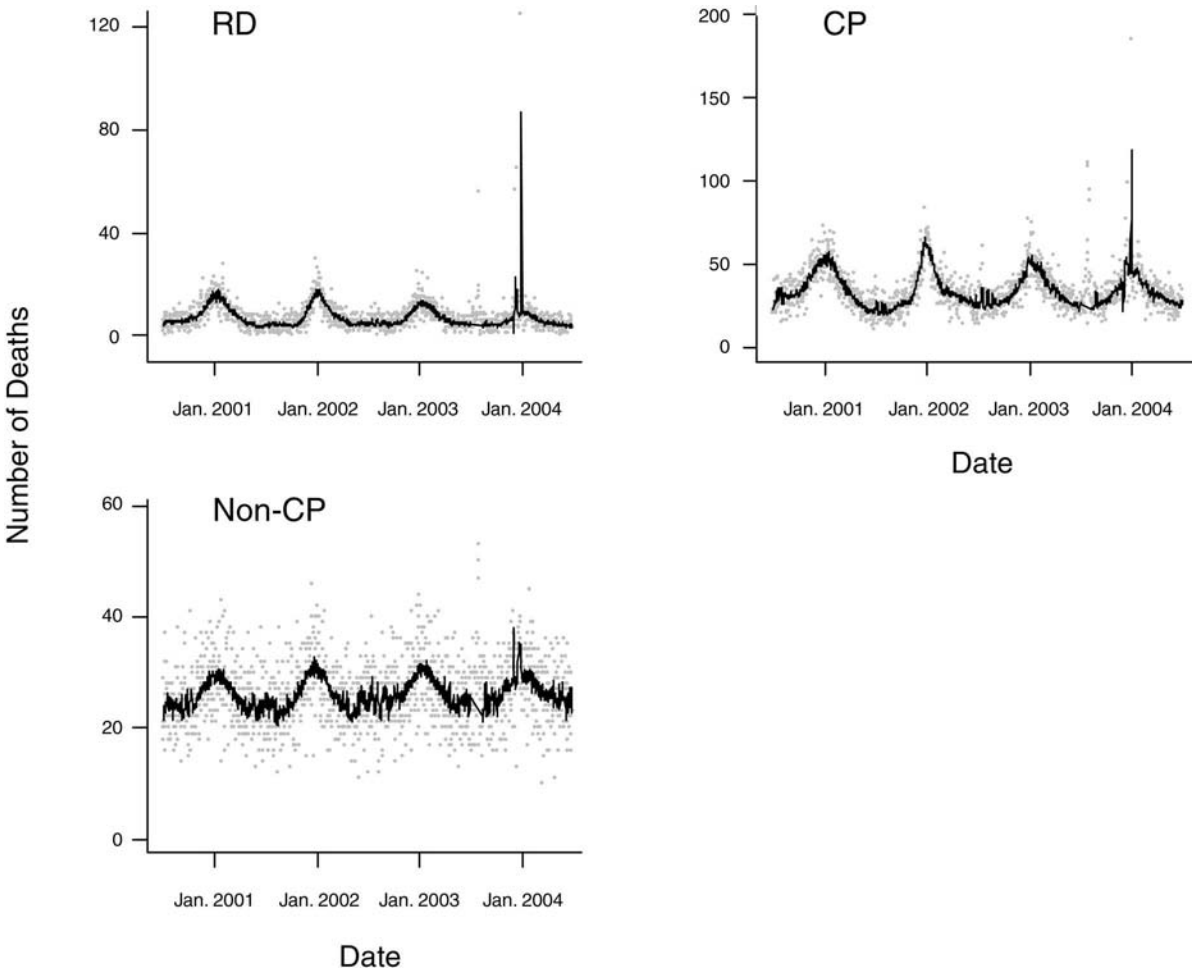


Figure 4D (*Continued*)

SENSITIVITY ANALYSES

The major purposes of the sensitivity analyses were to determine whether the results were stable and whether they were greatly affected by decisions made during the model construction. Therefore, we performed a wide range of sensitivity analyses, as described in Appendix A, to be certain that valid results were obtained.

SUBGROUP ANALYSES

To assess whether putatively susceptible subgroups (e.g., those aged ≥ 65) have a higher sensitivity to the effect of air pollution, we used individual-level information and performed stratified analyses for age and sex, respectively (see Appendix A).

ADDITIONAL ANALYSIS OF ICD CODING

In this study, both ICD-9 and ICD-10 coding was used to indicate the causes of mortality in Wuhan during the four-year study period from July 1, 2000, to June 30, 2004. The change from ICD-9 to ICD-10 coding happened on January 1, 2003. To assess the uncertainty that may be associated with a change from ICD-9-coded mortality data to ICD-10-coded mortality data, we required each district's center for disease control to code 2002 mortality data with ICD-10 coding, thus providing both ICD-9- and ICD-10-coded mortality data for the year 2002. We then analyzed the two sets of data for any potential differences in pollution mortality estimates caused by the shift in ICD coding (see Appendix A for details).

RESULTS

HEALTH EFFECTS OF PM_{10}

Based on the Common Protocol (found at the end of this volume), we calculated the daily arithmetic means of pollutant concentrations for the whole city using the simple averaging method. The monitor-specific percentage of valid daily measures of pollutants is shown in Table C.1 in Appendix C. Because O_3 measurements collected by the monitor situated at station 6 and then moved to station 7 did not meet the quality-assurance criteria set by the Common Protocol (i.e., valid O_3 samples were obtained for less than 75% of the days in a year), we excluded the O_3 data from this monitor from all subsequent analyses. We also excluded SO_2 measurements from the Wugang monitor (station 4) because it measured the highest daily mean concentrations of SO_2 (see Table C.7 in Appendix C), and the weakest correlations were between SO_2 measurements at this monitor and SO_2 measured at any other monitor. This is because a big ferrous smelter is located in the Wugang district, which consumes a large amount of coal and emits high levels of SO_2 into the air.

The distributions of the daily mean ambient concentrations of the study pollutants are shown in Table 4. The arithmetic mean of daily concentrations was 141.8 μg/m^3 for PM_{10}, 85.7 μg/m^3 for O_3, 39.2 μg/m^3 for SO_2, and 51.8 μg/m^3 for NO_2. Based on our review of the literature, the pollutant concentration ranges were wider and the upper ends of the ranges were higher in this study than those in other major published studies (Daniels et al. 2000; Qian et al. 2000). This feature of the pollutant ranges presents an ideal study opportunity to explore the exposure–effect relations between ambient air pollution and daily mortality.

We compared the distributions of the concentrations of the study pollutants using both the centering approach specified in the Common Protocol and the simple averaging approach; the results are shown in Tables C.2 and C.3 in Appendix C. These two approaches produced very similar distributions. The distribution similarity supports the use of either approach to calculate daily mean concentrations of the study pollutants as surrogate exposure variables in estimating the mortality health effect for the whole study population. We chose to use the simple averaging method. Distributions of monitor-specific pollution data are shown in Tables C.4 through C.9, which are found in Appendix C.

During the course of the study period, daily mean concentrations of PM_{10} and O_3 decreased, but the SO_2 and NO_2 concentrations increased (Table 5). There were considerable temporal variations in the daily mean concentrations during the four-year study period (Figure 5). The time-series plots in Figure 5 show that seasonal cycles accounted for much of the variability, although the annual changes were also important. PM_{10}, SO_2, and NO_2 had peaks in the winters. For O_3, as expected, peaks occurred in the summer months. Spatial variations of daily mean concentrations were also observed (Table 5). Time-series plots of monitor-specific PM_{10}, O_3, SO_2, and NO_2 daily mean concentrations are shown in Appendix D. Again, the highest daily mean concentrations of SO_2 were found at

Table 4. Distribution of Daily Mean Ambient Air Pollutant Concentrations and Weather Variables Used in Statistical Analyses, July 1, 2000, to June 30, 2004

Pollutant (μg/m^3) / Weather Variable	Number of Monitoring Stations	Number of Days of Measurements	Mean (SD)	Minimum	Maximum	Percentile		
						25th	50th	75th
PM_{10}	5	1458	141.8 (63.7)	24.8	477.8	94.8	130.2	175.0
NO_2	5	1457	51.8 (18.8)	19.2	127.4	38.0	47.2	62.0
SO_2[a]	4	1457	39.2 (25.3)	5.3	187.8	21.0	32.5	51.8
O_3[b]	1	1386	85.7 (47.0)	1.0	258.5	51.1	81.8	118.5
Daily mean temperature (˚C)	1	1461	17.9 (9.2)	−2.5	35.8	9.7	18.5	26.0
Daily mean relative humidity (%)	1	1461	74.0 (12.5)	35.0	99.0	65.0	74.0	84.0

[a] Excluding the station 4 (Wugang) monitor.

[b] Only station 5 (Donghu) provided valid measurements of O_3; daily 8-hour concentrations (10:00–18:00) were used.

Table 5. Correlations and Trends in Measured Ambient Air Pollutant Concentrations, July 1, 2000, to June 30, 2004

Pollutant ($\mu g/m^3$)	Number of Monitoring Stations	Range of Mean Values Between Stations	Coefficient of Variation of Daily Mean (%)	Range of Pearson Correlation Coefficients Between Monitoring Stations	Means of Daily Means	
					Mean	Average Annual Change[a]
PM_{10}	5	113.9–161.6	44.9	0.83–0.97	141.8	−4.3
NO_2	5	35.8–63.6	36.2	0.59–0.84	51.8	2.0
SO_2[b]	4	32.7–45.6	64.5	0.63–0.84	39.2	3.2
O_3[c]	1	NA	54.9	NA	85.7	−2.5

[a] Calculated from a linear regression model.

[b] Excluding the station 4 (Wugang) monitor.

[c] Only monitoring station 5 (Donghu) provided valid measurements of O_3; daily 8-hour concentrations (10:00–18:00) were used.

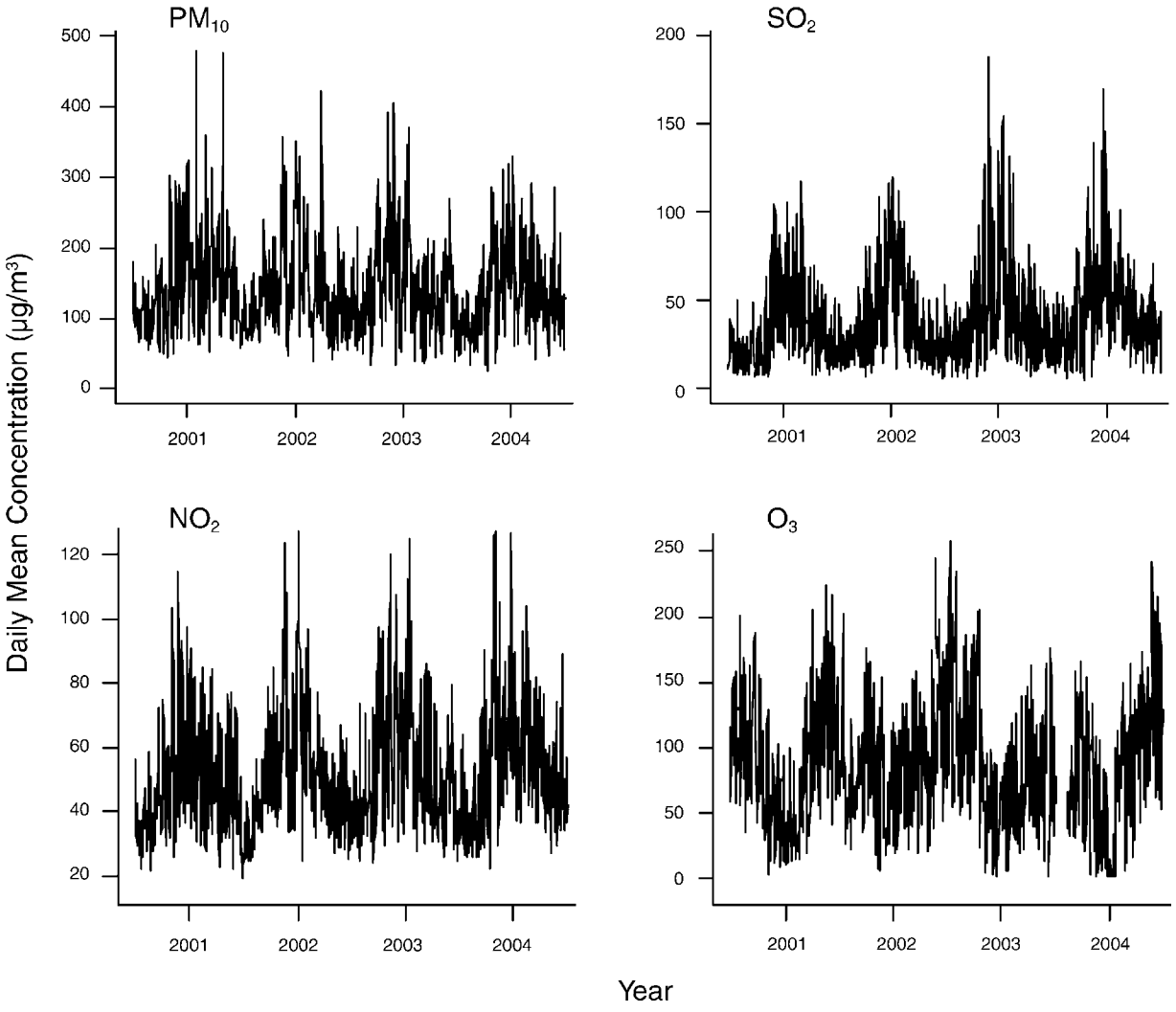


Figure 5. Time-series plots of daily mean concentrations of pollutants.

station 4 (Wugang). Table 6 shows correlations between pollutants averaged across monitors with seasonal corrections. Moderate correlations were found between PM_{10} and NO_2 (the correlation coefficient was 0.59) and between NO_2 and SO_2 (0.57). Weak correlations were found between O_3 and PM_{10} (0.09), between O_3 and SO_2 (0.16), and between O_3 and NO_2 (0.20). Monitor-to-monitor Pearson correlations within specific pollutants as well as between pollutants are shown in Tables C.15 and C.16 in Appendix C.

Table 4 shows the distribution of daily average temperature and daily average RH in Wuhan. During the study period, the daily average temperature ranged from −2.5 to 35.8°C. These results confirm that there is a large temperature difference between winter and summer in Wuhan. The daily average RH ranged from 35% to 99%. The time-series plots of the weather variables are shown in Figure 6.

We collected information on a total of 89,131 deaths attributed to natural causes during the study period (Table 7). The daily mean number of deaths due to all natural causes was 61.0, with the main contribution coming from CP mortality (mean of 34.9). Slightly more males (55.5% of total

Table 6. Correlations Between Pollutants Averaged Across Monitors with Seasonal Corrections, July 1, 2000, to June 30, 2004[a]

Pollutant	Partial Correlation Coefficient (*r*)
PM_{10}	
NO_2	0.59
SO_2	0.29
O_3[b]	0.09
NO_2	
SO_2	0.57
O_3	0.20
SO_2[c]	
O_3	0.16

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; and local smoothing over 2 peaks of mortality and the remaining period.

[b] Only monitoring station 5 (Donghu) provided valid measurements of O_3; daily 8-hour concentrations (10:00–18:00) were used.

[c] Excluding monitoring station 4 (Wugang).

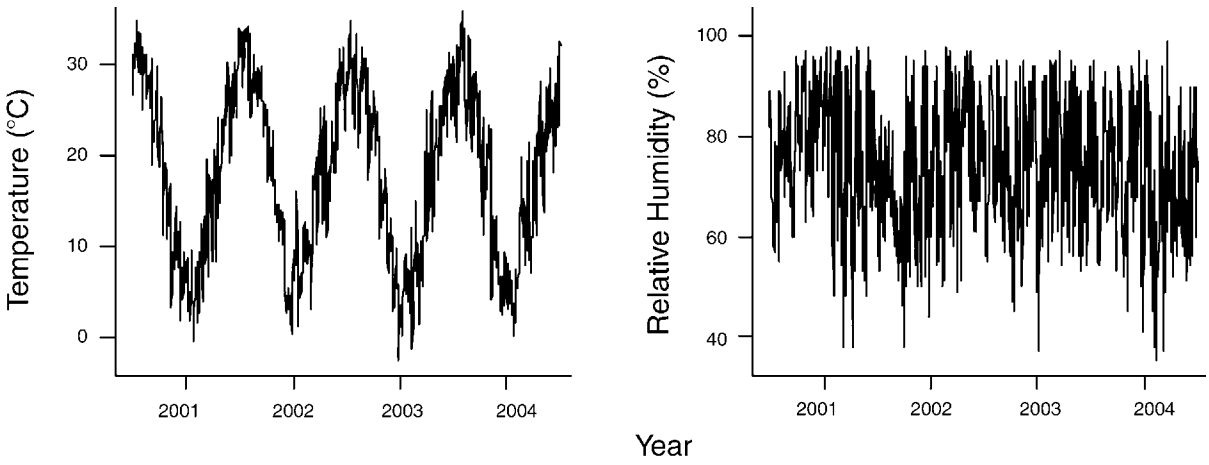


Figure 6. Time-series plots of daily mean weather measurements.

Table 7. Daily Mortality by Cause of Death and Sex, July 1, 2000, to June 30, 2004

Cause of Death[a]	Total Number of Deaths	Number of Days with No Deaths	Mean	Variance	Variance/ Mean	Minimum	Maximum	Percentile		
								25th	50th	75th
All natural	89,131	0	61.0	248.9	4.08	25	213	51	59	69
Males	49,457	0	33.9	83.8	2.48	12	109	27	33	39
Females	39,674	0	27.2	73.6	2.71	9	104	21	26	31
Cardiovascular	40,623	0	27.8	77.9	2.80	8	94	22	27	33
Males	20,957	0	14.3	27.4	1.91	2	46	11	14	17
Females	19,666	0	13.5	26.2	1.94	2	53	10	13	16
Stroke	25,557	0	17.5	34.8	1.99	4	57	13	17	21
Males	13,491	0	9.2	14.1	1.53	1	29	7	9	12
Females	12,066	0	8.3	12.1	1.47	1	36	6	8	10
Cardiac	12,166	2	8.3	13.8	1.66	0	29	6	8	11
Males	6,145	34	4.2	5.7	1.34	0	13	2	4	6
Females	6,021	40	4.1	5.6	1.35	0	21	2	4	5
Respiratory	10,287	9	7.0	33.4	4.75	0	125	4	6	9
Males	5,945	66	4.1	10.8	2.65	0	63	2	3	5
Females	4,342	140	3.0	9.5	3.18	0	62	1	2	4
Cardiopulmonary	50,910	0	34.9	159.1	4.56	11	185	27	32	41
Males	26,902	0	18.4	50.9	2.76	4	94	13	18	22
Females	24,008	0	16.4	47.3	2.88	2	91	12	15	19
Non-cardiopulmonary	38,221	0	26.2	34.2	1.31	10	53	22	26	30
Males	22,555	0	15.4	17.5	1.13	4	33	12	15	18
Females	15,666	0	10.7	12.3	1.15	2	31	8	10	13

[a] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

nonaccidental deaths) died than females. Among all natural deaths, over one-half were attributable to CP (57%). Most individuals in this category died when they were ≥ 65 years old (71.9%) (Tables C.11, C.12, and C.14). Persons who were ≥ 65 years in age contributed to more than half of the daily deaths for each of the underlying causes of death (Tables C.11 and C.14). The percentage of deaths in the group from 0 to 4 years old was 1.5% (Table C.12). In this age group, the total number of deaths was too small to conduct subsequent regression analyses. The time-series plots of daily mortality are shown in Figure 7. Mortality was overdispersed across the three temperature groups, since most of the variances were greater than the means (Table 7), and none of the time-series models were underdispersed.

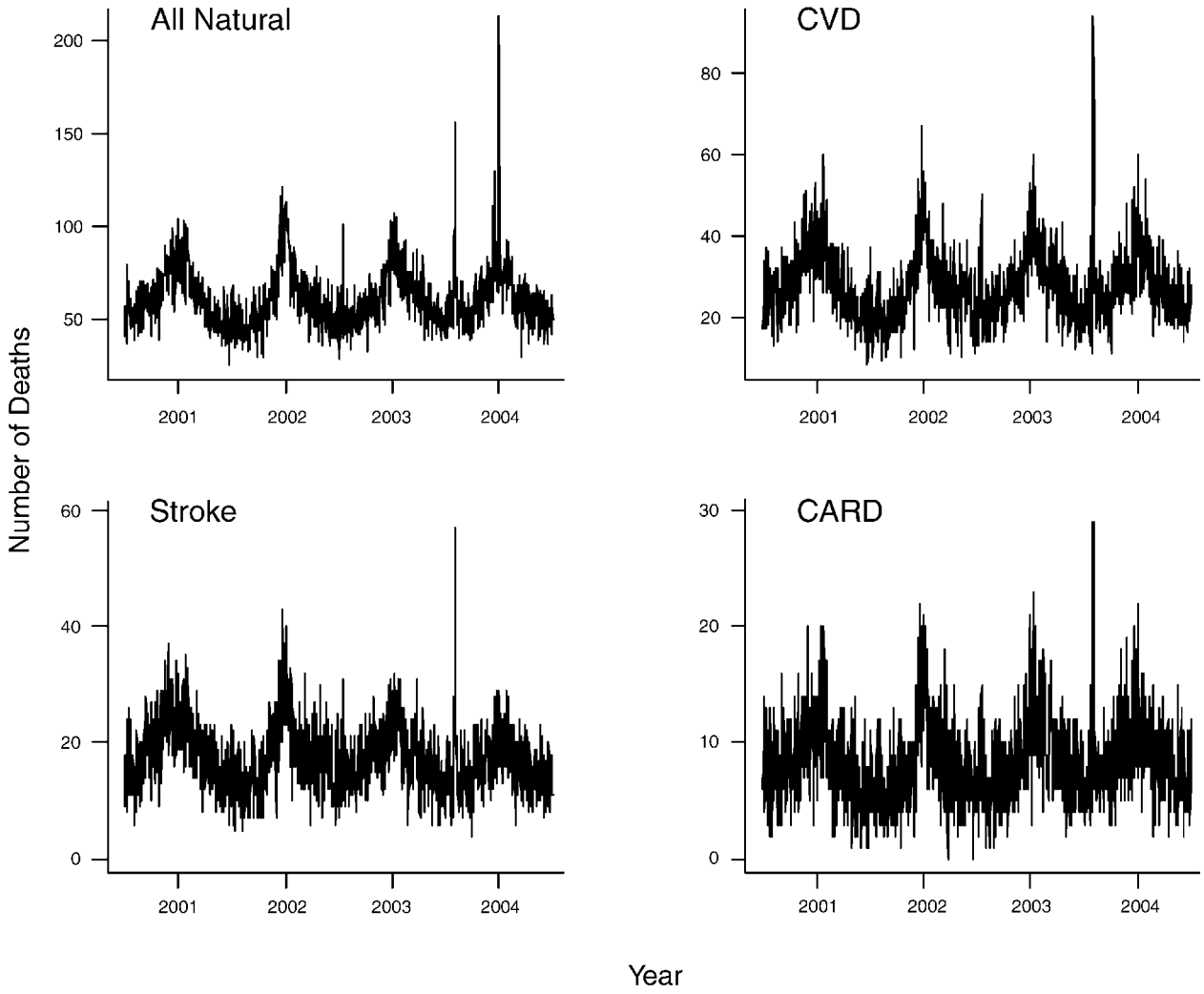


Figure 7. Time-series plots of daily mortality by cause of death.

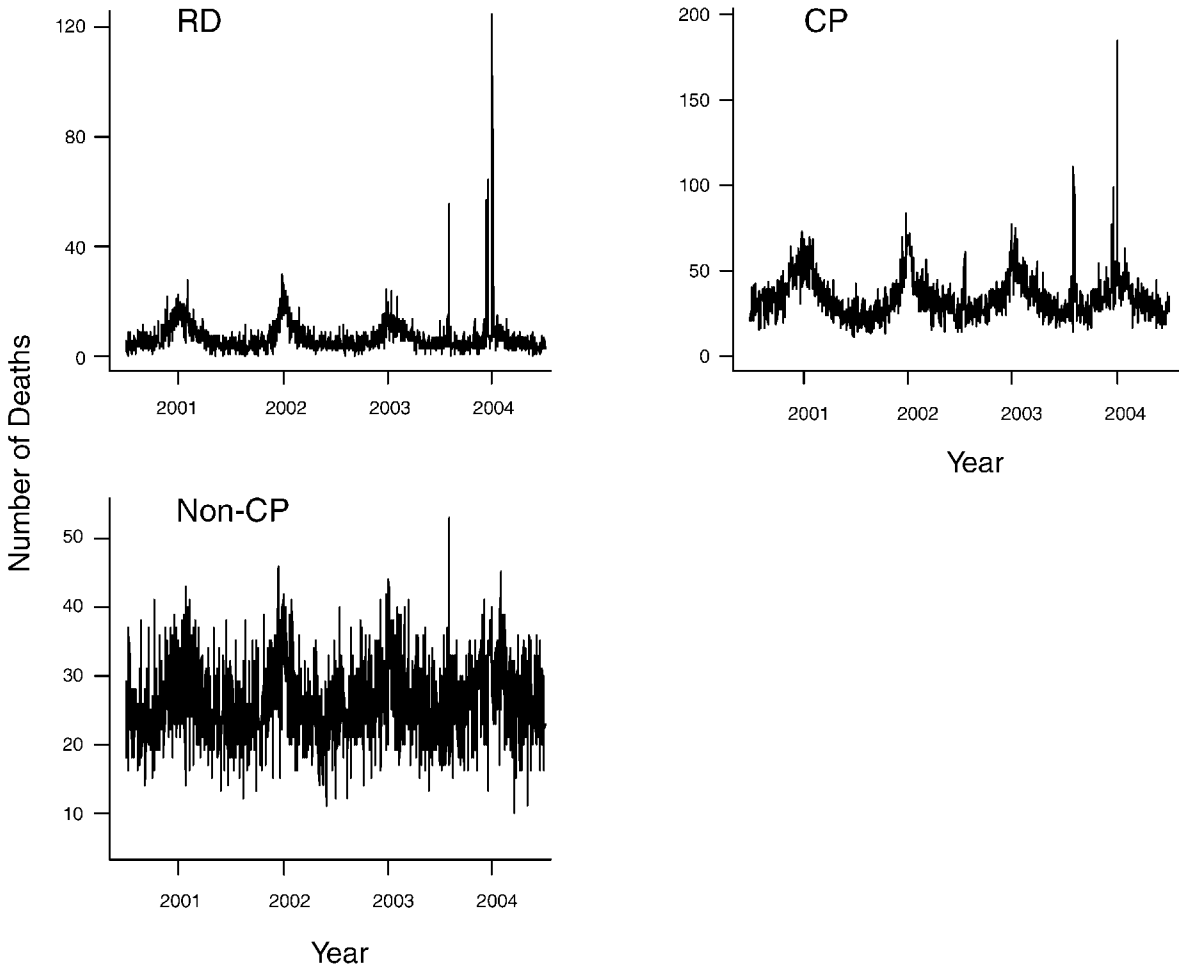


Figure 7 (*Continued*).

Table 8. Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in PM_{10} Concentration, by Sex, July 1, 2000, to June 30, 2004[a]

Cause of Death	Lag 0 Day Mean % Change (95% CI)	Lag 1 Day Mean % Change (95% CI)	Lag 0–1 Days[b] Mean % Change (95% CI)	Lag 0–4 Days[c] Mean % Change (95% CI)
All natural	0.36 (0.19 to 0.53)	0.28 (0.12 to 0.44)	0.43 (0.24 to 0.62)	0.08 (−0.14 to 0.31)
Males	0.32 (0.11 to 0.54)	0.24 (0.04 to 0.45)	0.39 (0.15 to 0.63)	0.00 (−0.28 to 0.29)
Females	0.41 (0.17 to 0.64)	0.32 (0.09 to 0.55)	0.47 (0.21 to 0.74)	0.17 (−0.14 to 0.49)
Cardiovascular	0.51 (0.27 to 0.74)	0.36 (0.13 to 0.58)	0.57 (0.31 to 0.84)	0.36 (0.06 to 0.67)
Males	0.41 (0.09 to 0.73)	0.30 (−0.01 to 0.61)	0.49 (0.13 to 0.85)	0.22 (−0.19 to 0.63)
Females	0.61 (0.29 to 0.93)	0.42 (0.11 to 0.72)	0.67 (0.31 to 1.02)	0.52 (0.11 to 0.93)
Stroke	0.43 (0.15 to 0.71)	0.40 (0.13 to 0.67)	0.57 (0.25 to 0.88)	0.44 (0.08 to 0.80)
Males	0.42 (0.04 to 0.80)	0.40 (0.03 to 0.76)	0.57 (0.15 to 1.00)	0.39 (−0.10 to 0.89)
Females	0.44 (0.04 to 0.83)	0.40 (0.03 to 0.78)	0.56 (0.12 to 1.00)	0.50 (−0.01 to 1.00)
Cardiac	0.48 (0.07 to 0.88)	0.29 (−0.10 to 0.68)	0.49 (0.04 to 0.94)	0.24 (−0.28 to 0.76)
Males	0.28 (−0.29 to 0.86)	0.12 (−0.43 to 0.68)	0.26 (−0.38 to 0.90)	0.04 (−0.69 to 0.78)
Females	0.68 (0.13 to 1.23)	0.45 (−0.07 to 0.98)	0.72 (0.11 to 1.32)	0.44 (−0.25 to 1.14)
Respiratory	0.77 (0.29 to 1.24)	0.61 (0.14 to 1.07)	0.87 (0.34 to 1.41)	0.30 (−0.33 to 0.93)
Males	0.57 (0.00 to 1.15)	0.46 (−0.09 to 1.02)	0.68 (0.04 to 1.32)	0.07 (−0.68 to 0.83)
Females	1.00 (0.30 to 1.70)	0.78 (0.11 to 1.46)	1.11 (0.32 to 1.90)	0.60 (−0.32 to 1.53)
Cardiopulmonary	0.46 (0.24 to 0.68)	0.33 (0.11 to 0.54)	0.52 (0.27 to 0.77)	0.13 (−0.16 to 0.43)
Males	0.31 (0.02 to 0.60)	0.22 (−0.06 to 0.50)	0.36 (0.03 to 0.69)	−0.13 (−0.52 to 0.26)
Females	0.63 (0.33 to 0.94)	0.45 (0.16 to 0.74)	0.70 (0.36 to 1.05)	0.44 (0.03 to 0.85)
Non-cardiopulmonary	0.24 (0.02 to 0.46)	0.23 (0.02 to 0.44)	0.30 (0.05 to 0.54)	−0.06 (−0.35 to 0.24)
Males	0.36 (0.07 to 0.65)	0.30 (0.02 to 0.57)	0.42 (0.10 to 0.74)	0.10 (−0.28 to 0.48)
Females	0.07 (−0.26 to 0.41)	0.13 (−0.19 to 0.45)	0.12 (−0.25 to 0.49)	−0.28 (−0.71 to 0.16)

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; and local smoothing over 2 peaks of mortality and the remaining period.

[b] The mean concentrations across the concurrent day and the one preceding day.

[c] The mean concentrations across the concurrent day and the four preceding days.

Table 8 shows the estimated effects on daily mortality of 10-μg/m^3 incremental increases in PM_{10} concentrations. Every 10-μg/m^3 increase in PM_{10} at lag 0–1 day was statistically significantly associated with an increase in all natural (0.43%; 95% CI, 0.24 to 0.62) deaths and deaths due specifically to CVD (0.57%; 95% CI, 0.31 to 0.84), stroke (0.57%; 95% CI, 0.25 to 0.88), CARD (0.49%; 95% CI, 0.04 to 0.94), RD (0.87%; 95% CI, 0.34 to 1.41), CP (0.52%; 95% CI, 0.27 to 0.77), and non-CP (0.30%; 95% CI, 0.05 to 0.54) causes. We stratified the data by sex and age to take a close look at the effects of PM_{10} at lag 0–1 day (Tables 8 and 9). The observed significant and positive associations in females were consistently stronger than in males with the exception of stroke and non-CP mortality (Table 8). Among individuals ≥ 65 years of age at the time of death, PM_{10} was statistically significantly associated with all cause-specific mortality except for non-CP mortality (Table 9).

Sensitivity analyses were conducted to assess whether the estimated effects were valid and whether they were

Table 9. Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in PM_{10} Concentration by Age, July 1, 2000, to June 30, 2004[a]

	Lag 0 Day	Lag 1 Day	Lag 0–1 Days[b]	Lag 0–4 Days[c]
Cause of Death / Age (Years)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural	0.36 (0.19 to 0.53)	0.28 (0.12 to 0.44)	0.43 (0.24 to 0.62)	0.08 (−0.14 to 0.31)
< 65	0.21 (−0.08 to 0.50)	0.24 (−0.04 to 0.52)	0.33 (0.01 to 0.65)	0.01 (−0.38 to 0.39)
≥ 65	0.42 (0.22 to 0.61)	0.29 (0.10 to 0.48)	0.46 (0.24 to 0.68)	0.10 (−0.16 to 0.37)
Cardiovascular	0.51 (0.27 to 0.74)	0.36 (0.13 to 0.58)	0.57 (0.31 to 0.84)	0.36 (0.06 to 0.67)
< 65	0.26 (−0.23 to 0.76)	0.33 (−0.14 to 0.80)	0.44 (−0.10 to 0.99)	0.49 (−0.14 to 1.12)
≥ 65	0.56 (0.30 to 0.83)	0.36 (0.11 to 0.61)	0.61 (0.31 to 0.90)	0.33 (0.00 to 0.67)
Stroke	0.43 (0.15 to 0.71)	0.40 (0.13 to 0.67)	0.57 (0.25 to 0.88)	0.44 (0.08 to 0.80)
< 65	0.24 (−0.37 to 0.86)	0.37 (−0.21 to 0.96)	0.46 (−0.21 to 1.15)	0.59 (−0.19 to 1.37)
≥ 65	0.47 (0.16 to 0.79)	0.41 (0.10 to 0.71)	0.59 (0.24 to 0.94)	0.41 (0.00 to 0.82)
Cardiac	0.48 (0.07 to 0.88)	0.29 (−0.10 to 0.68)	0.49 (0.04 to 0.94)	0.24 (−0.28 to 0.76)
< 65	0.00 (−0.90 to 0.90)	0.16 (−0.70 to 1.02)	0.16 (−0.84 to 1.16)	0.15 (−0.99 to 1.31)
≥ 65	0.59 (0.15 to 1.03)	0.32 (−0.10 to 0.74)	0.56 (0.08 to 1.05)	0.26 (−0.29 to 0.82)
Respiratory	0.77 (0.29 to 1.24)	0.61 (0.14 to 1.07)	0.87 (0.34 to 1.41)	0.30 (−0.33 to 0.93)
< 65	0.15 (−1.17 to 1.48)	−0.58 (−1.86 to 0.72)	−0.29 (−1.77 to 1.21)	−0.44 (−2.15 to 1.29)
≥ 65	0.84 (0.35 to 1.33)	0.74 (0.27 to 1.22)	1.01 (0.46 to 1.56)	0.38 (−0.26 to 1.03)
Cardiopulmonary	0.46 (0.24 to 0.68)	0.33 (0.11 to 0.54)	0.52 (0.27 to 0.77)	0.13 (−0.16 to 0.43)
< 65	0.14 (−0.33 to 0.61)	0.13 (−0.32 to 0.58)	0.21 (−0.32 to 0.74)	0.15 (−0.47 to 0.78)
≥ 65	0.53 (0.29 to 0.77)	0.37 (0.14 to 0.61)	0.59 (0.31 to 0.86)	0.13 (−0.20 to 0.46)
Non-cardiopulmonary	0.24 (0.02 to 0.46)	0.23 (0.02 to 0.44)	0.30 (0.05 to 0.54)	−0.06 (−0.35 to 0.24)
< 65	0.19 (−0.15 to 0.53)	0.25 (−0.07 to 0.57)	0.30 (−0.08 to 0.68)	−0.20 (−0.64 to 0.25)
≥ 65	0.27 (−0.02 to 0.57)	0.21 (−0.07 to 0.49)	0.29 (−0.03 to 0.62)	0.04 (−0.34 to 0.42)

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; and local smoothing over 2 peaks of mortality and the remaining period.

[b] The mean concentrations across the concurrent day and the one preceding day.

[c] The mean concentrations across the concurrent day and the four preceding days.

strongly influenced by different model specifications during the modeling process. As the sensitivity analyses were rather extensive, we focused on the effects of PM_{10} at lag 0–1 day. In general, using different smoothing approaches did not change the statistical significance of the effect estimates, nor did using different model specifications. The maximum changes in PM_{10} effect estimates using different smoothing approaches and different model specifications were less than 0.3% (Figure 8) and 0.2% (Figure 9), respectively. The results of two-pollutant models are shown in Table 10. Both NO_2 and SO_2 reduced the effects of PM_{10} on most categories of daily mortality at lag 0–1 day, but O_3 did not.

These estimated PM_{10} effects were based on the assumption that the fitted exposure–response function was consistent with a linear function. To examine this assumption, we obtained the smoothed exposure–response curves for all cause-specific mortality for lag 0–1 day by using a smoothed model that specified a smooth function for PM_{10} with 3 degrees of freedom (df) (Figure 10). For all natural,

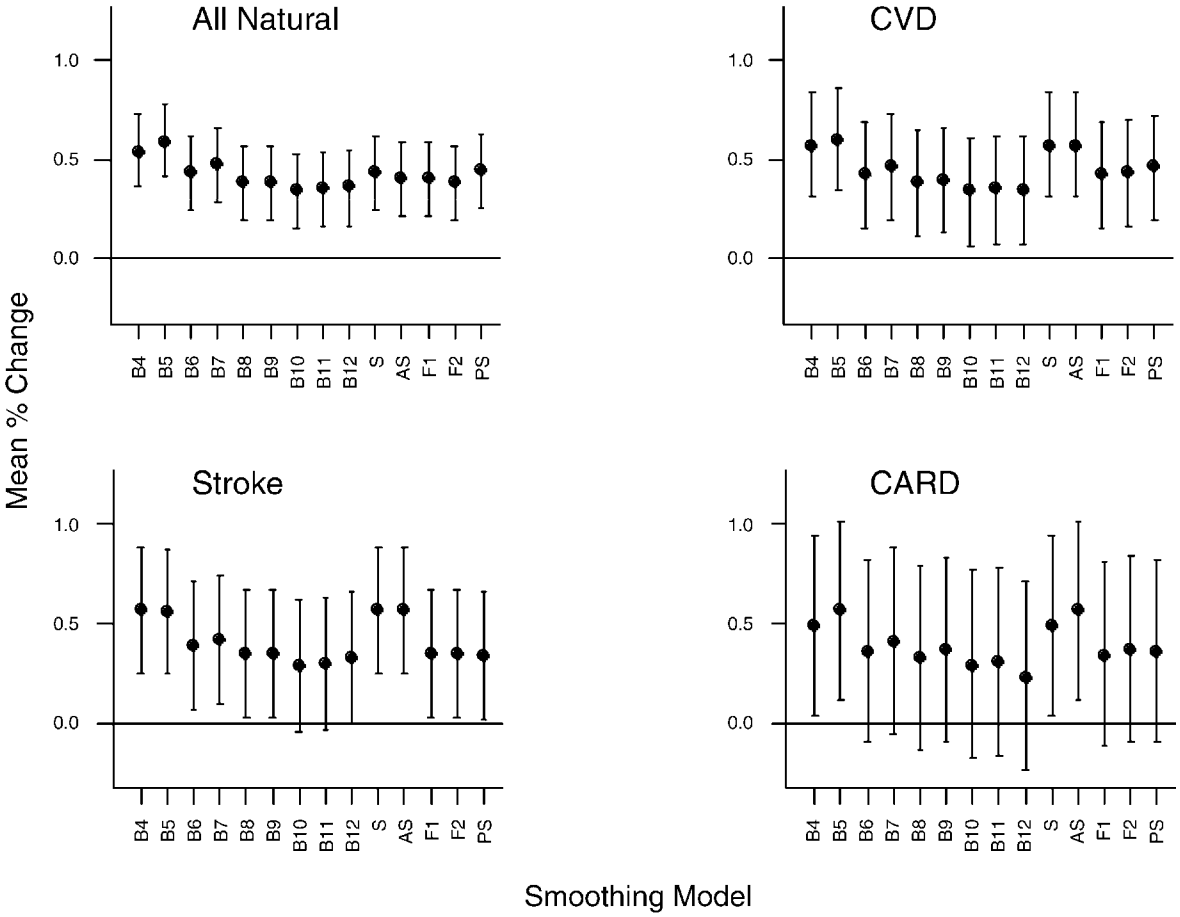
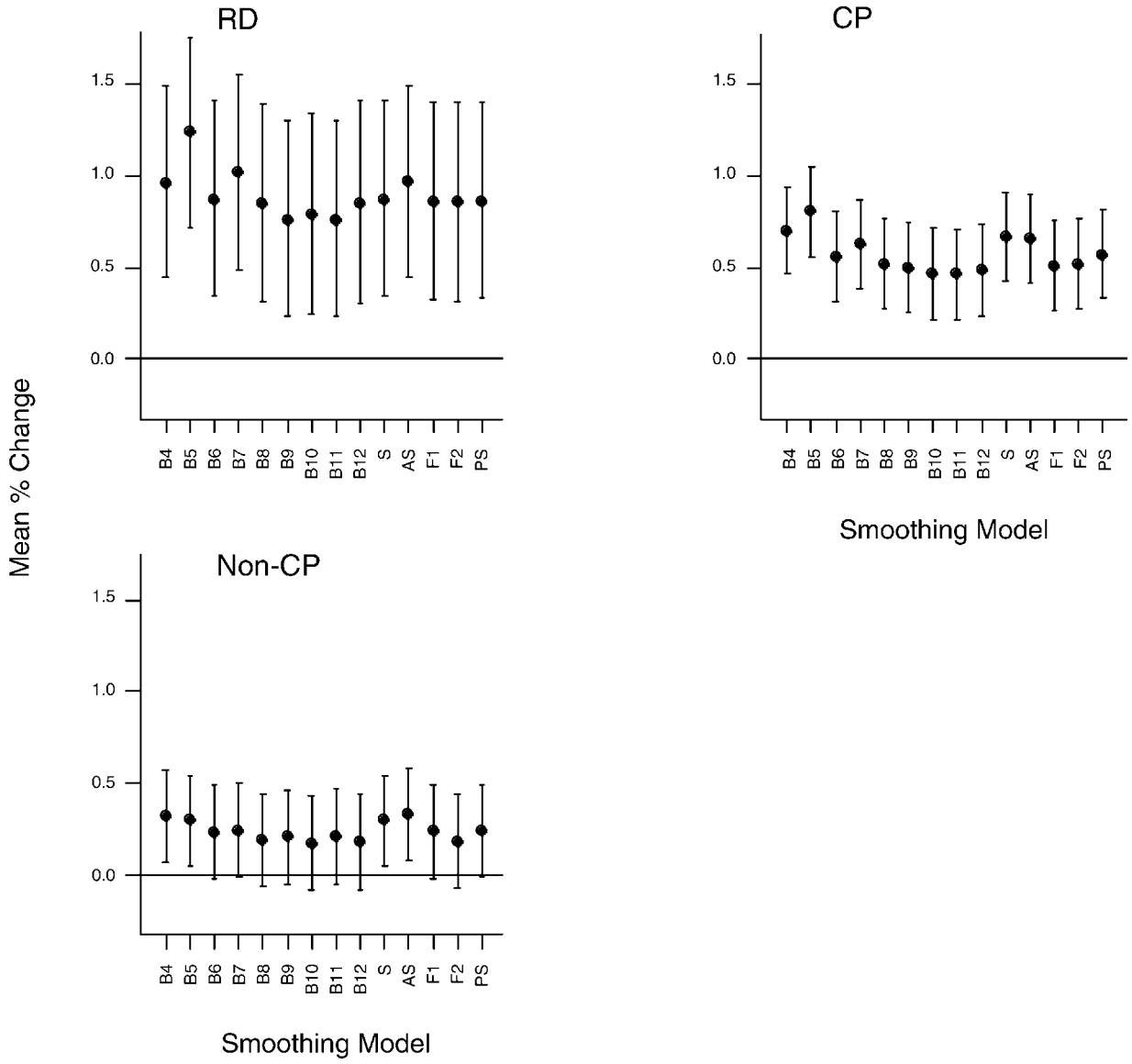


Figure 8. Sensitivity analyses for different smoothing approaches for PM_{10} at lag 0–1 day by cause of death. B4–B12 indicate the best model with increasing degrees of freedom for the time smoothing function; S indicates the sequential method final model; AS indicates the alternate sequential method final model; F1 indicates the natural spline model 1 with fixed degrees of freedom; F2 indicates the natural spline model 2 with fixed degrees of freedom; and PS indicates the penalized spline method final model.



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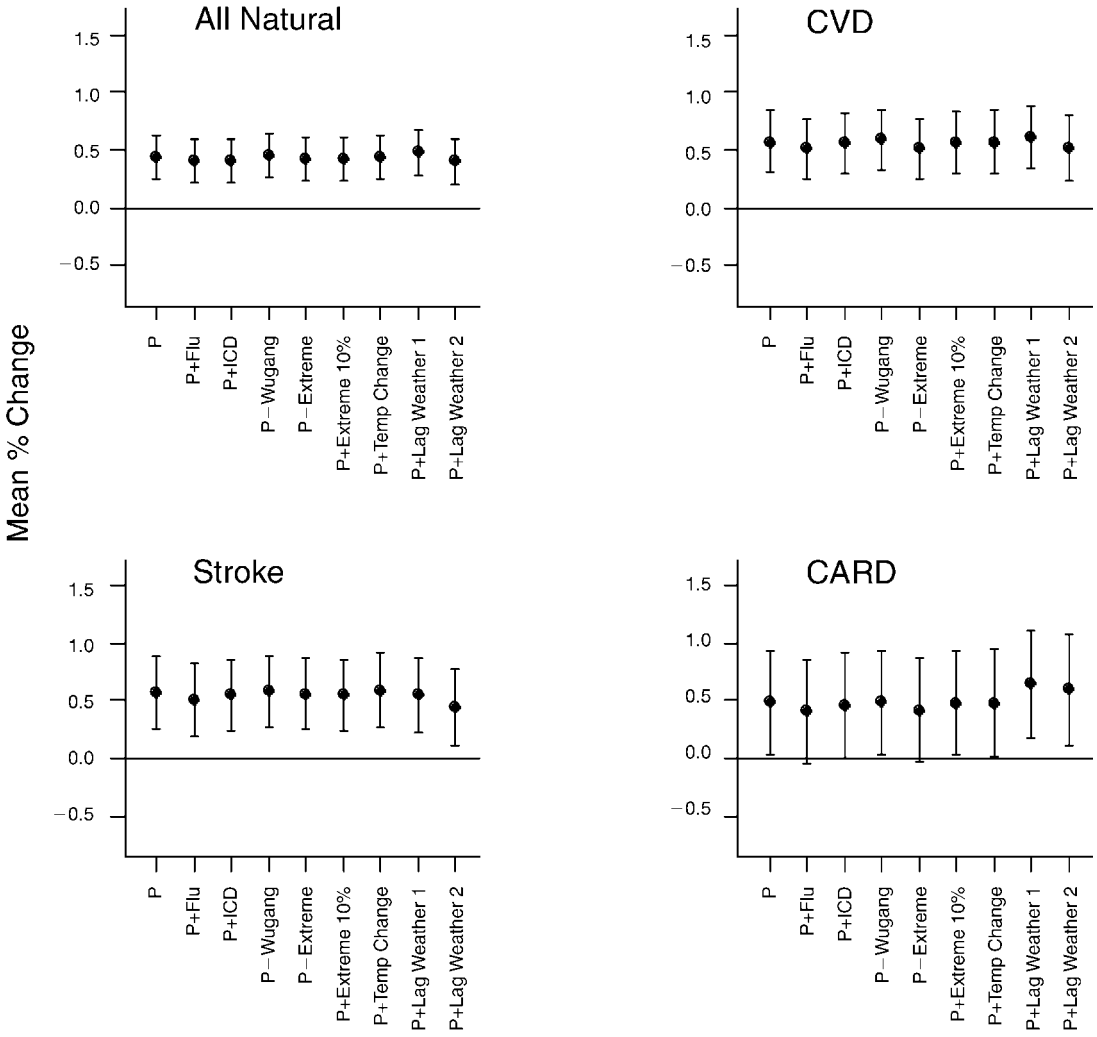

Figure 9. Sensitivity analyses for different model specifications for PM_{10} at lag 0–1 day by cause of death. P indicates primary model; P+Flu indicates variable for flu season as a potential confounder; P+ICD indicates adding ICD indicator; P−Wugang indicates excluding the monitor in Wugang district (station 4); P−Extreme indicates excluding extreme weather indicators; P+Extreme 10% indicates using extreme weather indicators based on 10th percentile; P+Temp Change indicates adding daily temperature change (high − low); P+Lag Weather 1 indicates adding lag 1–2 day mean for weather terms; and P+Lag Weather 2 indicates adding lag 1–2 day mean and lag 3–7 day mean for weather terms.

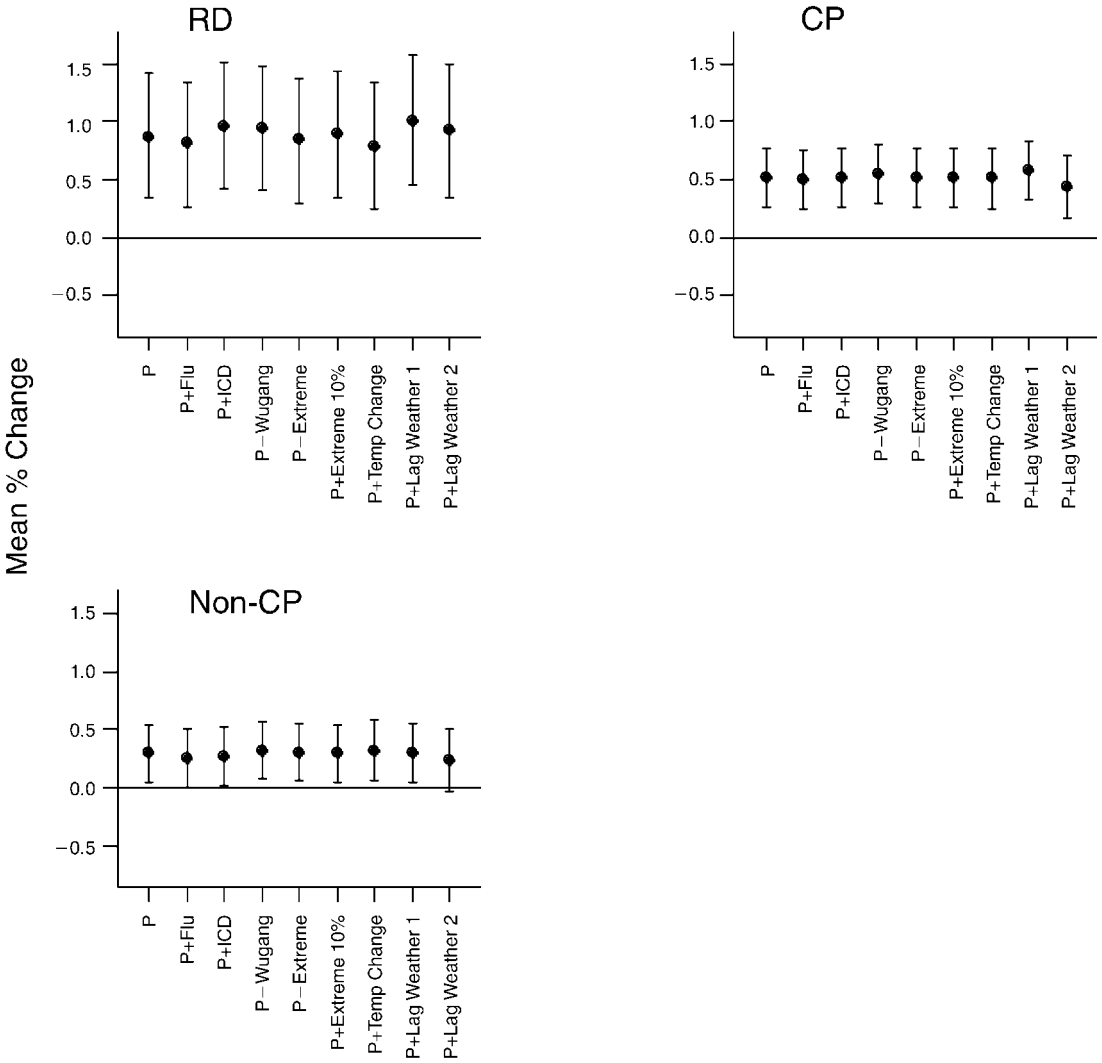

Figure 9 (*Continued*).

Table 10. Two-Pollutant Regression Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in PM_{10} Concentration for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a]

Cause of Death / Pollutant(s)	Mean % Change (95% CI)
All natural	
PM_{10}	0.43 (0.24 to 0.62)
$PM_{10} + NO_2$	0.13 (−0.10 to 0.37)
$PM_{10} + SO_2$	0.33 (0.13 to 0.52)
$PM_{10} + O_3$	0.43 (0.23 to 0.62)
Cardiovascular	
PM_{10}	0.57 (0.31 to 0.84)
$PM_{10} + NO_2$	0.33 (0.00 to 0.66)
$PM_{10} + SO_2$	0.46 (0.18 to 0.74)
$PM_{10} + O_3$	0.56 (0.28 to 0.83)
Stroke	
PM_{10}	0.57 (0.25 to 0.88)
$PM_{10} + NO_2$	0.31 (−0.08 to 0.70)
$PM_{10} + SO_2$	0.50 (0.17 to 0.83)
$PM_{10} + O_3$	0.51 (0.19 to 0.83)
Cardiac	
PM_{10}	0.49 (0.04 to 0.94)
$PM_{10} + NO_2$	0.21 (−0.35 to 0.78)
$PM_{10} + SO_2$	0.29 (−0.19 to 0.77)
$PM_{10} + O_3$	0.53 (0.07 to 1.00)
Respiratory	
PM_{10}	0.87 (0.34 to 1.41)
$PM_{10} + NO_2$	0.39 (−0.29 to 1.07)
$PM_{10} + SO_2$	0.70 (0.14 to 1.27)
$PM_{10} + O_3$	0.90 (0.34 to 1.45)
Cardiopulmonary	
PM_{10}	0.52 (0.27 to 0.77)
$PM_{10} + NO_2$	0.23 (−0.09 to 0.54)
$PM_{10} + SO_2$	0.41 (0.15 to 0.68)
$PM_{10} + O_3$	0.53 (0.27 to 0.78)
Non-cardiopulmonary	
PM_{10}	0.30 (0.05 to 0.54)
$PM_{10} + NO_2$	0.01 (−0.30 to 0.32)
$PM_{10} + SO_2$	0.20 (−0.06 to 0.46)
$PM_{10} + O_3$	0.34 (0.08 to 0.60)

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; and local smoothing over 2 peaks of mortality and the remaining period.

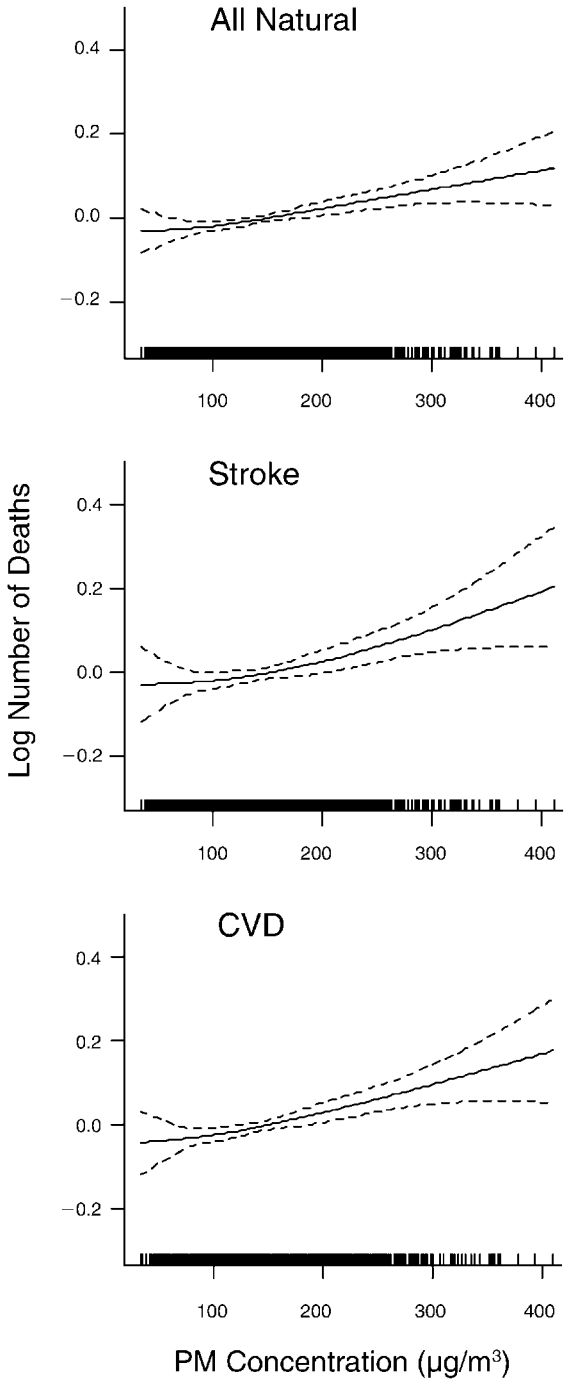

Figure 10. Exposure–response curves for the mean percentage of change in mortality evaluated at lag 0–1 day for PM_{10} concentrations by cause of death using 3 df. The solid lines represent the estimated mean percentage of change. The dotted lines represent the 95% CIs.

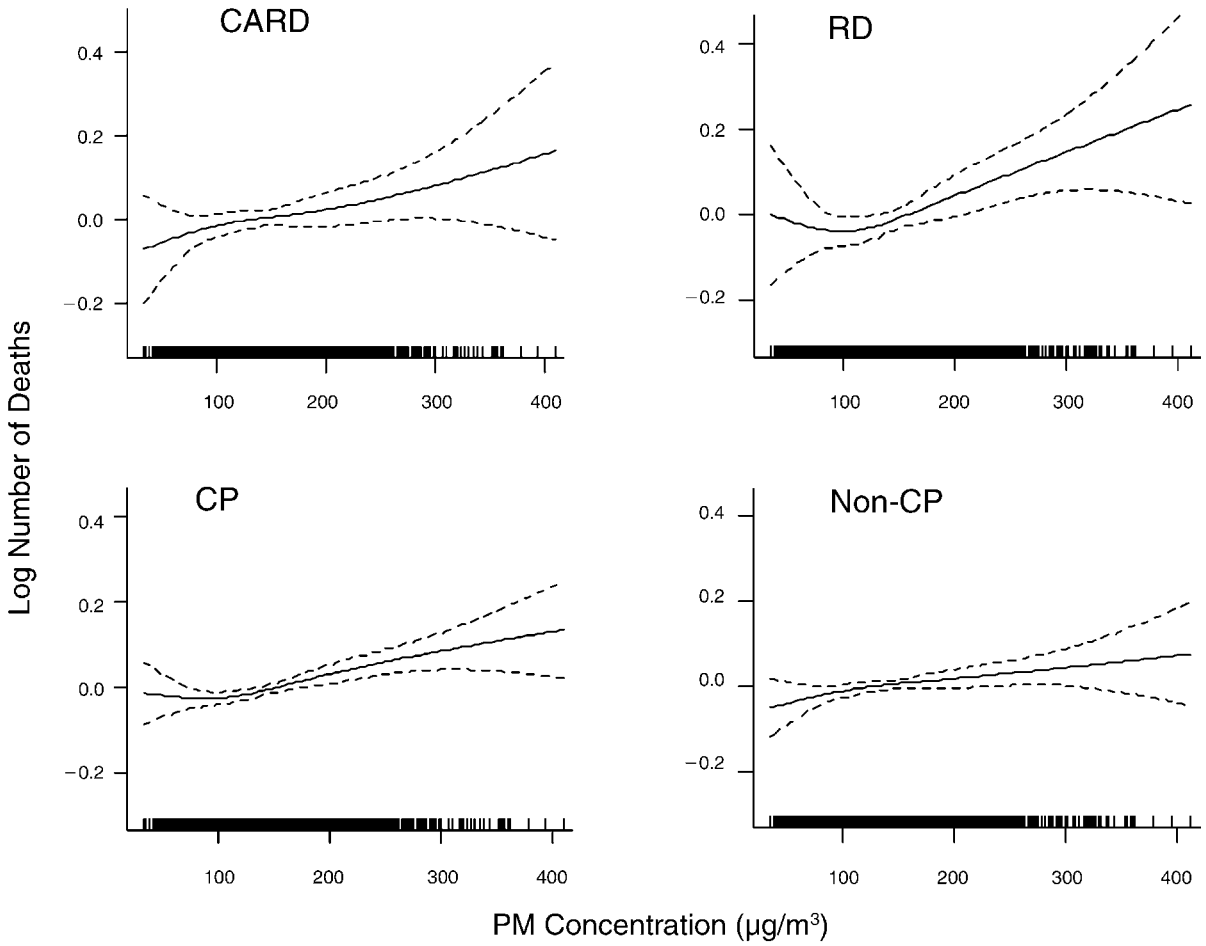

Figure 10 (*Continued*).

CVD, stroke, CARD, and non-CP causes of mortality, the smoothed curves are fairly linear and consistent with the absence of a threshold. Slight differences in curves were observed for RD and CARD mortality. For RD mortality, there appears to be little increase in risk until the PM_{10} concentration exceeds approximately 120 µg/m^3. For CP mortality, there is some evidence of an increased effect of PM_{10}, again above the concentration of 120 µg/m^3.

Table 11 shows the generalized cross-validation (GCV) values for mortality due to all natural causes and cause-specific mortality for lag 0–1 day under the smoothed, linear, and piecewise exposure–response models. In general, the GCV values are very similar up to the second decimal point, and the smallest GCV values tend to correspond to very low concentrations of PM_{10}. Furthermore, the results of the likelihood ratio test that compared the linear model with the smoothed model (allowing nonlinearity of the relations) were not statistically significant, thus suggesting the appropriateness of assuming a linear relation between daily mortality and PM_{10}. This evaluation is generally consistent with the visual assessment of the smoothed exposure–response curves for cause-specific mortality.

HEALTH EFFECTS OF GASEOUS POLLUTANTS

Based on the Common Protocol, we conducted separate analyses for the three gaseous pollutants: NO_2, SO_2, and O_3. We examined the mortality effects of each pollutant at lag 0, lag 1, lag 2, lag 3, and lag 4 days, and the 2-day (lag 0–1) and 4-day (lag 0–3) means. For the purposes of this report, we focused on the results at lag 0–1 day. Tables 12 and 13 show the mean percentage change in daily mortality per 10-µg/m^3 increase in concentrations of NO_2, SO_2, and O_3 by sex and age, respectively. Across mortality due to all natural causes and all categories of cause-specific mortality, we found consistent elevations in daily mortality for increased NO_2 and SO_2, but not for O_3. These associations

Table 11. Generalized Cross-Validation Statistics for Various Regression Models for PM_{10} for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a]

	Regression Model							
Cause of Death	Smoothed	Linear	PW50	PW75	PW100	PW125	PW150	*P* Value[b]
All natural	1.385292	1.381913	1.376436	1.382097	1.383625	1.383744	1.383899	0.167
Cardiovascular	1.316557	1.313185	1.310737	1.313877	1.315015	1.314445	1.314995	0.685
Stroke	1.143099	1.141403	1.139052	1.141867	1.142710	1.141643	1.142343	0.471
Cardiac	1.140677	1.137717	1.139170	1.139356	1.138867	1.139299	1.139183	0.879
Respiratory	1.409889	1.406064	1.406630	1.408084	1.406248	1.406275	1.407921	0.142
Cardiopulmonary	1.395889	1.392498	1.386053	1.391854	1.393511	1.392923	1.394489	0.165
Non-cardiopulmonary	1.057643	1.054457	1.054556	1.055924	1.055711	1.054859	1.055525	0.509

[a] The models included the base model plus different specifications of the PM_{10} relationship to the logarithm of cause-specific mortality (i.e., log(death) = base model + f(PM_{10})). The "smoothed" model specified a smooth function for PM_{10} (df = 3), and the "linear" model specified a linear function for PM_{10}. The piecewise regression (PW) model allowed the slope of PM_{10} to change after the cutoff point at concentration x (x = 50, 75, 100, 125, and 150 μg/m^3, respectively).

[b] *P* value for testing whether the "smoothed" model significantly improved model fit from the "linear" model using the likelihood ratio test (df = 2).

Table 12. Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in Concentrations of Gaseous Pollutants for Lag 0–1 Day by Sex, July 1, 2000, to June 30, 2004[a]

	NO_2	SO_2	O_3
Cause of Death / Sex	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural	1.96 (1.30 to 2.62)	1.20 (0.66 to 1.74)	0.29 (−0.05 to 0.63)
Males	1.83 (0.98 to 2.68)	0.95 (0.26 to 1.65)	0.22 (−0.21 to 0.66)
Females	2.13 (1.20 to 3.06)	1.51 (0.76 to 2.27)	0.37 (−0.10 to 0.85)
Cardiovascular	2.12 (1.18 to 3.06)	1.47 (0.70 to 2.25)	−0.07 (−0.53 to 0.39)
Males	1.95 (0.69 to 3.22)	1.17 (0.13 to 2.23)	−0.18 (−0.80 to 0.44)
Females	2.30 (1.05 to 3.57)	1.80 (0.76 to 2.85)	0.05 (−0.57 to 0.66)
Stroke	2.17 (1.07 to 3.28)	1.10 (0.19 to 2.02)	−0.08 (−0.61 to 0.45)
Males	2.36 (0.86 to 3.88)	0.80 (−0.44 to 2.05)	−0.23 (−0.96 to 0.51)
Females	1.94 (0.40 to 3.51)	1.44 (0.16 to 2.74)	0.08 (−0.67 to 0.83)
Cardiac	2.02 (0.44 to 3.62)	2.04 (0.74 to 3.37)	−0.48 (−1.26 to 0.30)
Males	0.79 (−1.41 to 3.05)	1.63 (−0.23 to 3.52)	−0.61 (−1.69 to 0.49)
Females	3.26 (1.13 to 5.44)	2.45 (0.69 to 4.24)	−0.36 (−1.42 to 0.70)
Respiratory	3.69 (1.78 to 5.64)	2.10 (0.58 to 3.63)	0.12 (−0.89 to 1.15)
Males	3.57 (1.28 to 5.90)	1.35 (−0.47 to 3.19)	0.51 (−0.70 to 1.72)
Females	3.82 (1.03 to 6.69)	3.07 (0.85 to 5.33)	−0.44 (−1.93 to 1.06)
Cardiopulmonary	2.17 (1.29 to 3.05)	1.33 (0.62 to 2.05)	0.15 (−0.30 to 0.61)
Males	1.90 (0.77 to 3.05)	0.96 (0.04 to 1.89)	0.07 (−0.52 to 0.66)
Females	2.47 (1.28 to 3.68)	1.75 (0.78 to 2.73)	0.24 (−0.38 to 0.87)
Non-cardiopulmonary	1.66 (0.79 to 2.53)	1.01 (0.29 to 1.73)	0.22 (−0.21 to 0.65)
Males	1.80 (0.68 to 2.94)	0.95 (0.01 to 1.90)	0.15 (−0.40 to 0.71)
Females	1.45 (0.15 to 2.77)	1.09 (0.02 to 2.18)	0.31 (−0.34 to 0.96)

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; and local smoothing over 2 peaks of mortality and the remaining period.

Table 13. Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in Concentrations of Gaseous Pollutants for Lag 0–1 Day by Age, July 1, 2000, to June 30, 2004[a]

	NO_2	SO_2	O_3
Cause of Death / Age (Years)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural	1.96 (1.30 to 2.62)	1.20 (0.66 to 1.74)	0.29 (−0.05 to 0.63)
< 65	1.13 (0.01 to 2.27)	0.51 (−0.41 to 1.45)	0.18 (−0.38 to 0.74)
≥ 65	2.26 (1.49 to 3.04)	1.45 (0.82 to 2.09)	0.33 (−0.07 to 0.73)
Cardiovascular	2.12 (1.18 to 3.06)	1.47 (0.70 to 2.25)	−0.07 (−0.53 to 0.39)
< 65	0.17 (−1.73 to 2.10)	0.45 (−1.14 to 2.07)	−0.16 (−1.08 to 0.78)
≥ 65	2.59 (1.56 to 3.63)	1.72 (0.86 to 2.58)	−0.05 (−0.56 to 0.46)
Stroke	2.17 (1.07 to 3.28)	1.10 (0.19 to 2.02)	−0.08 (−0.61 to 0.45)
< 65	0.01 (−2.34 to 2.42)	−0.18 (−2.15 to 1.83)	−0.72 (−1.86 to 0.42)
≥ 65	2.71 (1.46 to 3.97)	1.42 (0.39 to 2.46)	0.08 (−0.52 to 0.69)
Cardiac	2.02 (0.44 to 3.62)	2.04 (0.74 to 3.37)	−0.48 (−1.26 to 0.30)
< 65	0.17 (−3.25 to 3.70)	1.84 (−1.04 to 4.80)	0.40 (−1.31 to 2.14)
≥ 65	2.44 (0.75 to 4.17)	2.09 (0.68 to 3.52)	−0.69 (−1.53 to 0.15)
Respiratory	3.69 (1.78 to 5.64)	2.10 (0.58 to 3.63)	0.12 (−0.89 to 1.15)
< 65	−0.33 (−5.40 to 5.01)	0.44 (−3.66 to 4.72)	−0.13 (−2.84 to 2.65)
≥ 65	4.16 (2.20 to 6.15)	2.32 (0.77 to 3.89)	0.13 (−0.92 to 1.19)
Cardiopulmonary	2.17 (1.29 to 3.05)	1.33 (0.62 to 2.05)	0.15 (−0.30 to 0.61)
< 65	−0.30 (−2.10 to 1.54)	0.25 (−1.24 to 1.76)	−0.02 (−0.95 to 0.92)
≥ 65	2.69 (1.74 to 3.65)	1.56 (0.78 to 2.34)	0.19 (−0.30 to 0.69)
Non-cardiopulmonary	1.66 (0.79 to 2.53)	1.01 (0.29 to 1.73)	0.22 (−0.21 to 0.65)
< 65	1.88 (0.56 to 3.22)	0.52 (−0.58 to 1.64)	0.24 (−0.40 to 0.88)
≥ 65	1.49 (0.36 to 2.64)	1.33 (0.39 to 2.28)	0.20 (−0.37 to 0.77)

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; and local smoothing over 2 peaks of mortality and the remaining period.

were generally stronger among females than males except for stroke and non-CP mortality with NO_2 (Table 12). Except for non-CP mortality with NO_2, we observed a consistently higher mean percentage of mortality changes in the analyses of NO_2 as well as SO_2 among persons ≥ 65 years of age (Table 13).

We conducted a series of sensitivity analyses and observed a slight decreasing trend in effects with an increase in degrees of freedom per year for the best main models for NO_2 (Figure 11) and SO_2 (Figure 12). In general, few important differences were observed among the estimated mean percentage of mortality changes for all categories of causes of mortality for these two pollutants. The sensitivity analyses were also extended to determine whether these results were modified by different model specifications. The results were fairly robust and did not alter the effect magnitude or statistical significance level for NO_2 (Figure 13) or SO_2 (Figure 14). However, both the addition of the lag 1–2 day mean for weather terms and the addition of the lag 1–2 day mean and lag 3–7 day mean for weather terms simultaneously greatly reduced the estimated effects — in most cases making the estimated effects statistically nonsignificant. Adding PM_{10} or SO_2 to the analysis changed the mean percentage of all categories of causes of daily mortality in the direction of decreasing the effects of NO_2 (Table 14). However, the statistically significant and positive associations between NO_2 and mortality still hold and were changed little by the inclusion of O_3. For SO_2, the inclusion of PM_{10} or NO_2 consistently decreased the estimated effects of SO_2 and made some of the SO_2 effects statistically insignificant (Table 15). For the estimated effects of O_3, inclusion of a copollutant did not change the statistically insignificant levels of the estimated effects (see Table E.2 in Appendix E).

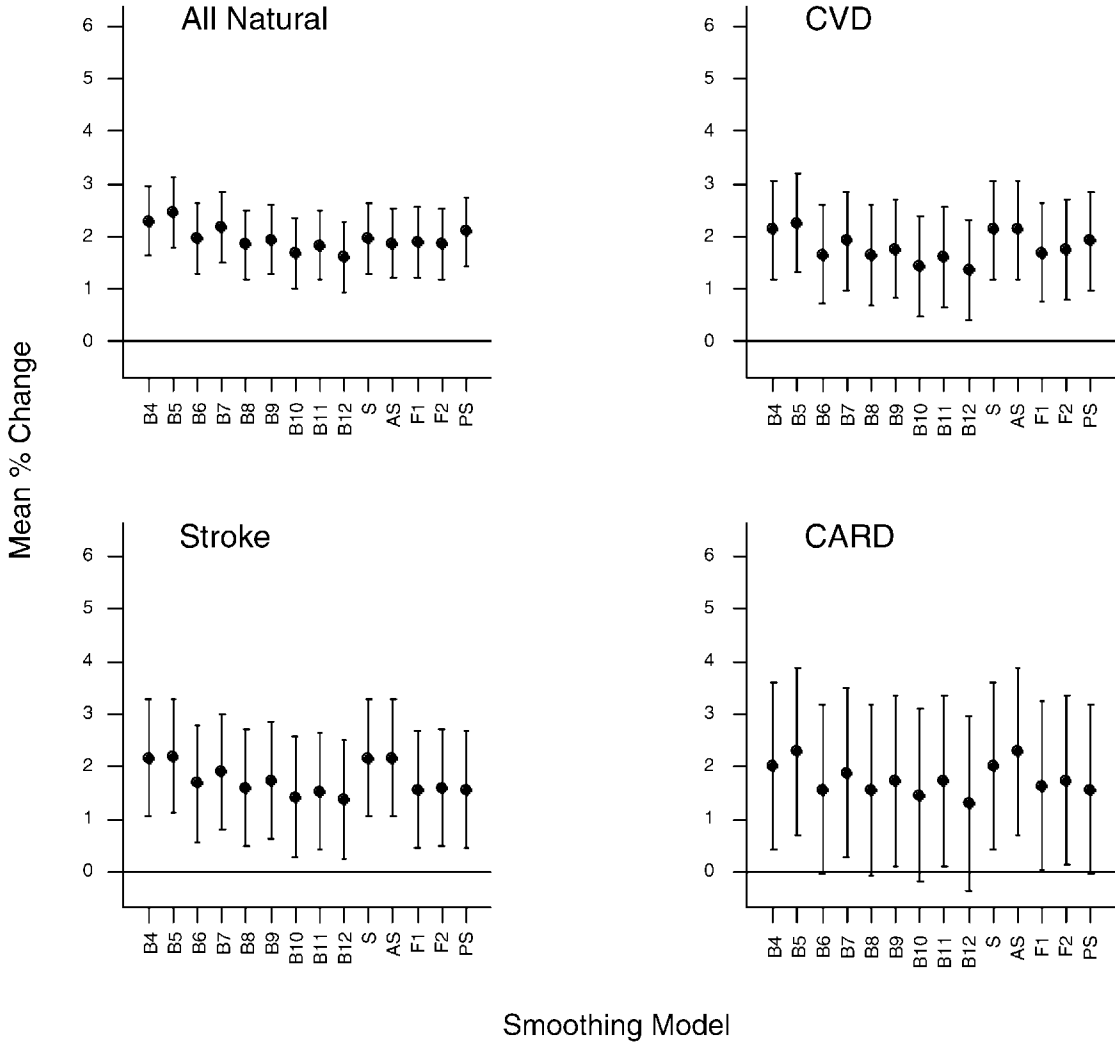

Figure 11. Sensitivity analyses for different smoothing approaches for NO_2 at lag 0–1 day by cause of death. B4–B12 indicate best model with increasing degrees of freedom for the time smoothing function; S indicates sequential method final model; AS indicates alternate sequential method final model; F1 indicates natural spline fixed degrees of freedom model 1; F2 indicates natural spline fixed degrees of freedom model 2; PS indicates penalized spline method final model.

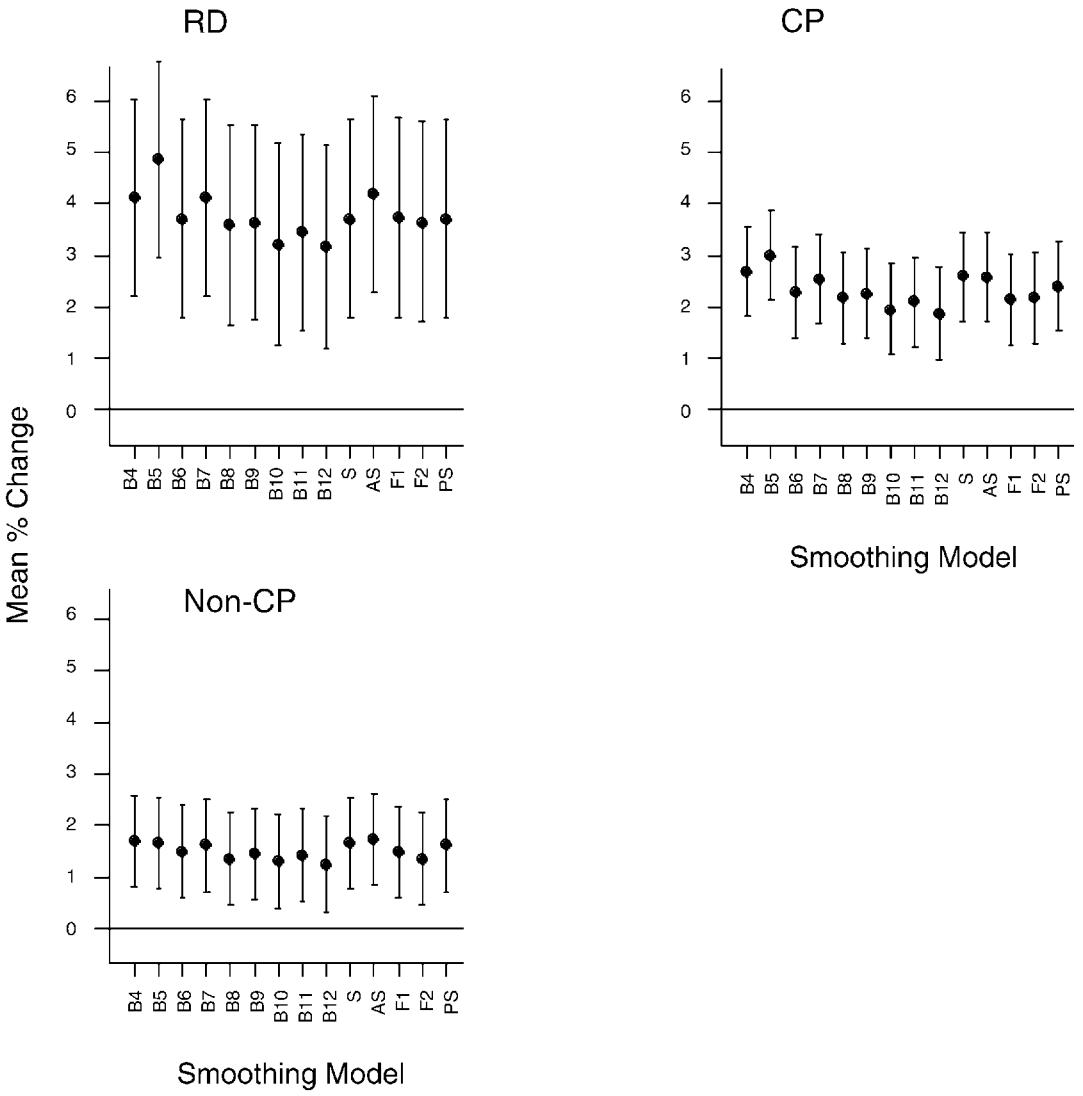

Figure 11 (*Continued*).

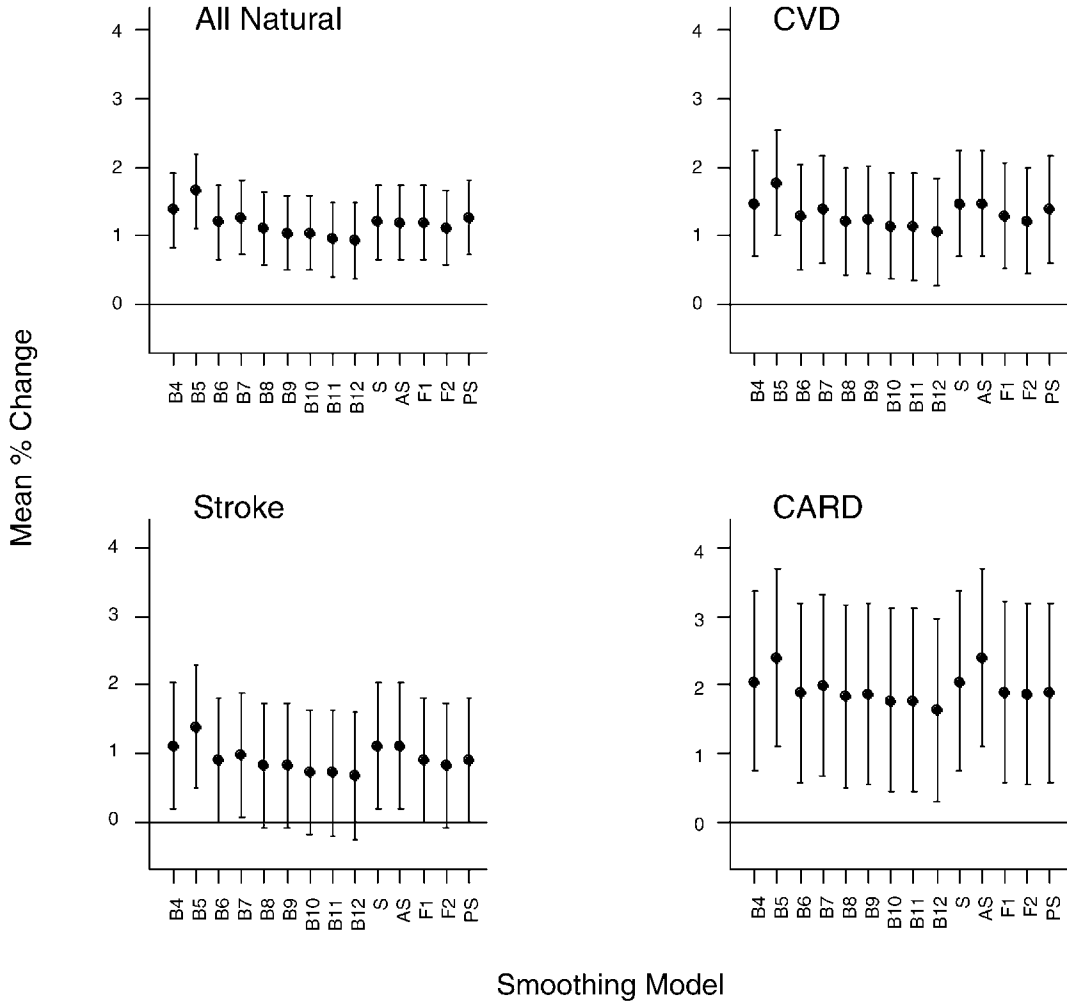

Figure 12. Sensitivity analyses for different smoothing approaches for SO_2 at lag 0–1 day by cause of death. B4–B12 indicate the best model with increasing degrees of freedom for the time smoothing function; S indicates sequential method final model; AS indicates alternate sequential method final model; F1 indicates natural spline fixed degrees of freedom model 1; F2 indicates natural spline fixed degrees of freedom model 2; and PS indicates penalized spline method final model.

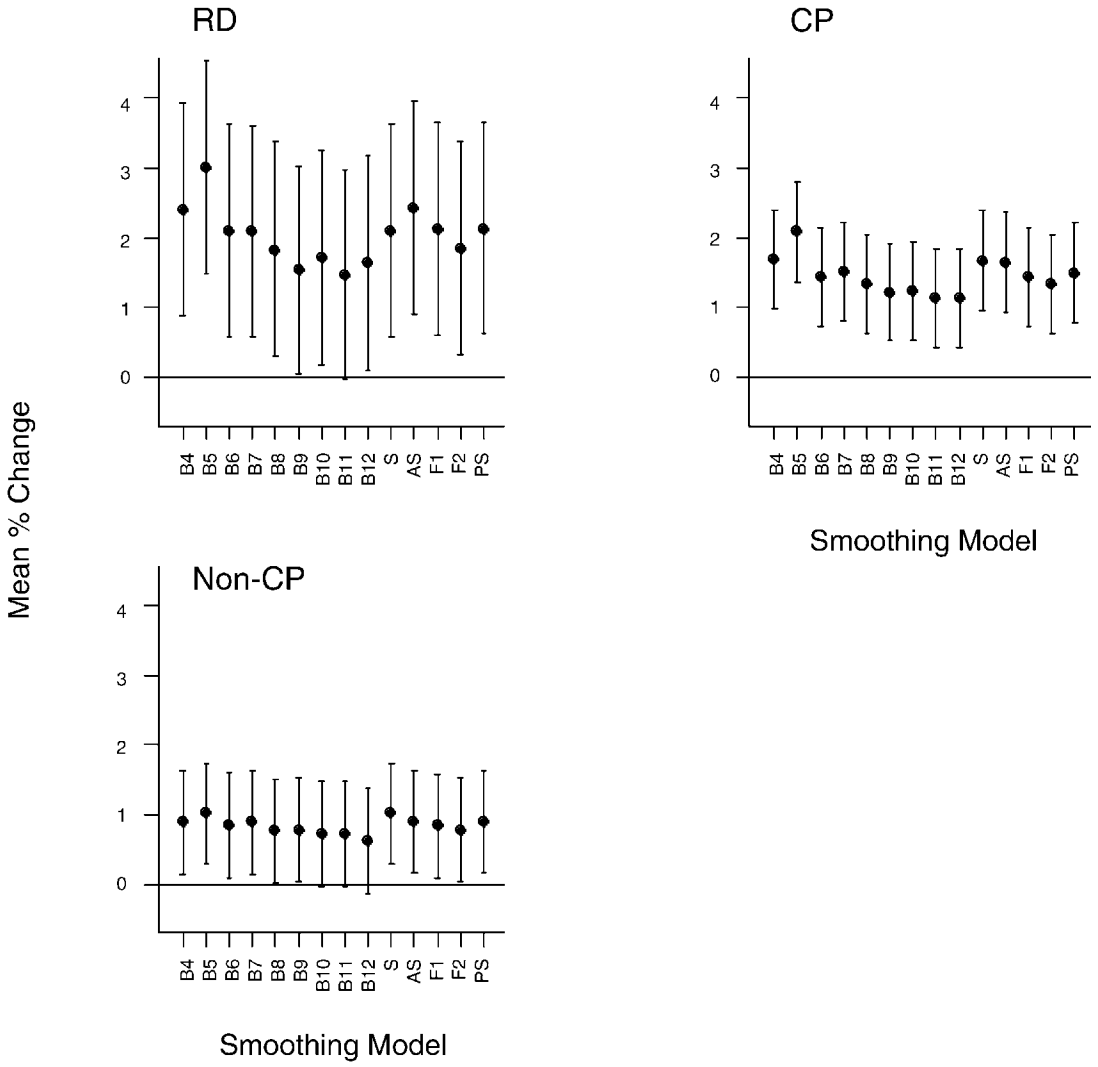

Figure 12 (*Continued*).

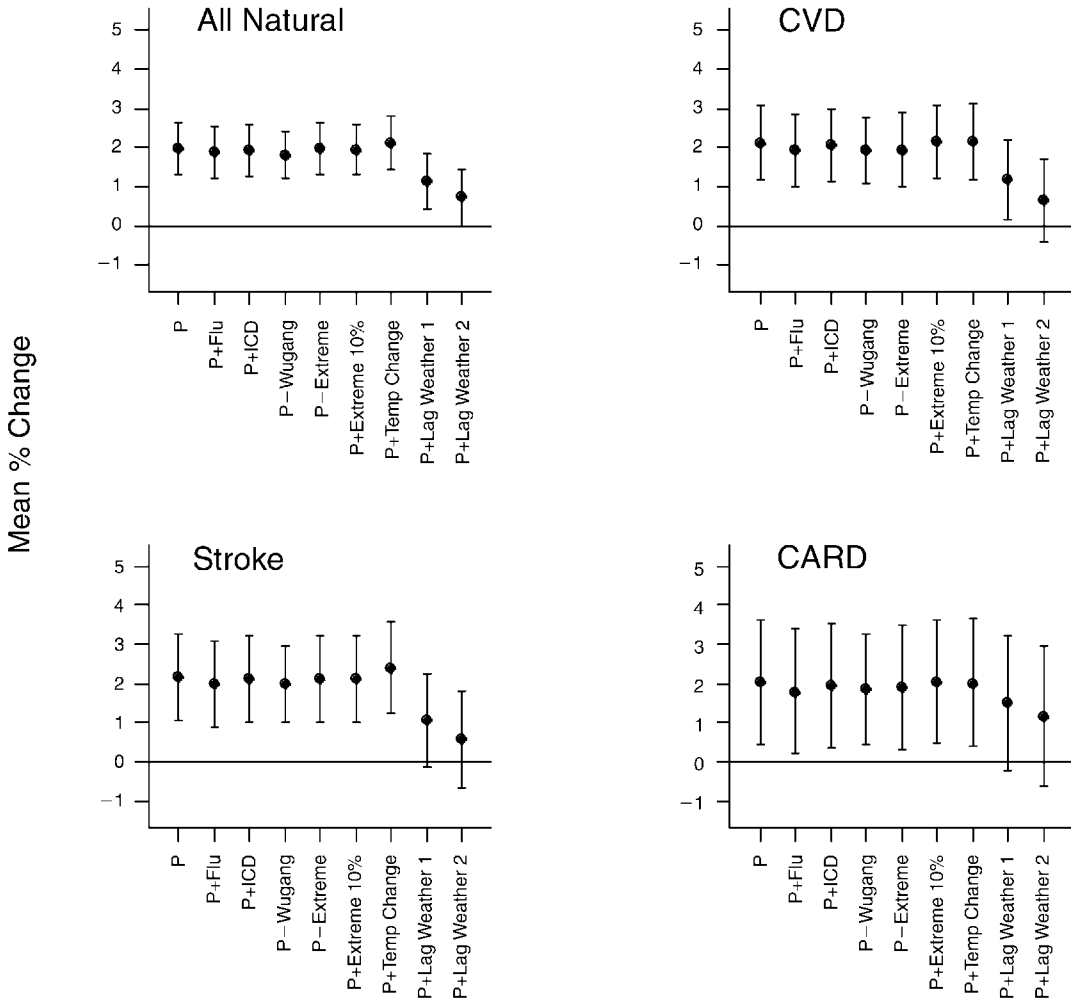

Figure 13. Sensitivity analyses for different model specifications for NO_2 at lag 0–1 day by cause of death. P indicates primary model; P+Flu indicates adding flu season; P+ICD indicates adding ICD indicator; P−Wugang (station 4) indicates excluding the monitor in Wugang district; P−Extreme indicates excluding extreme weather indicators; P+Extreme 10% indicates using extreme weather indicators based on 10th percentile; P+Temp Change indicates adding daily temperature change (high − low); P+Lag Weather 1 indicates adding lag 1–2 day mean for weather terms; and P+Lag Weather 2 indicates adding lag 1–2 day mean and lag 3–7 day mean for weather terms.

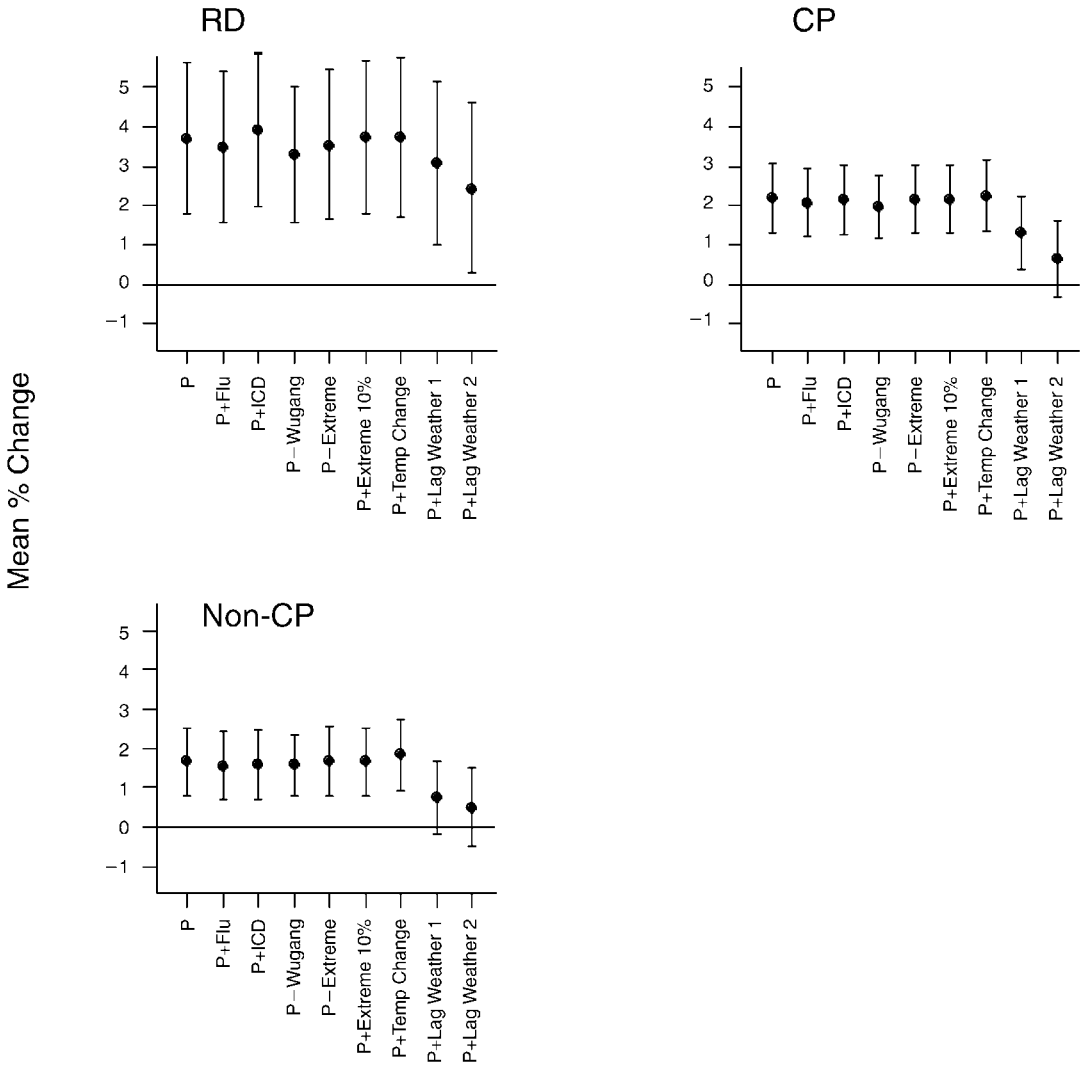

Figure 13 (*Continued*).

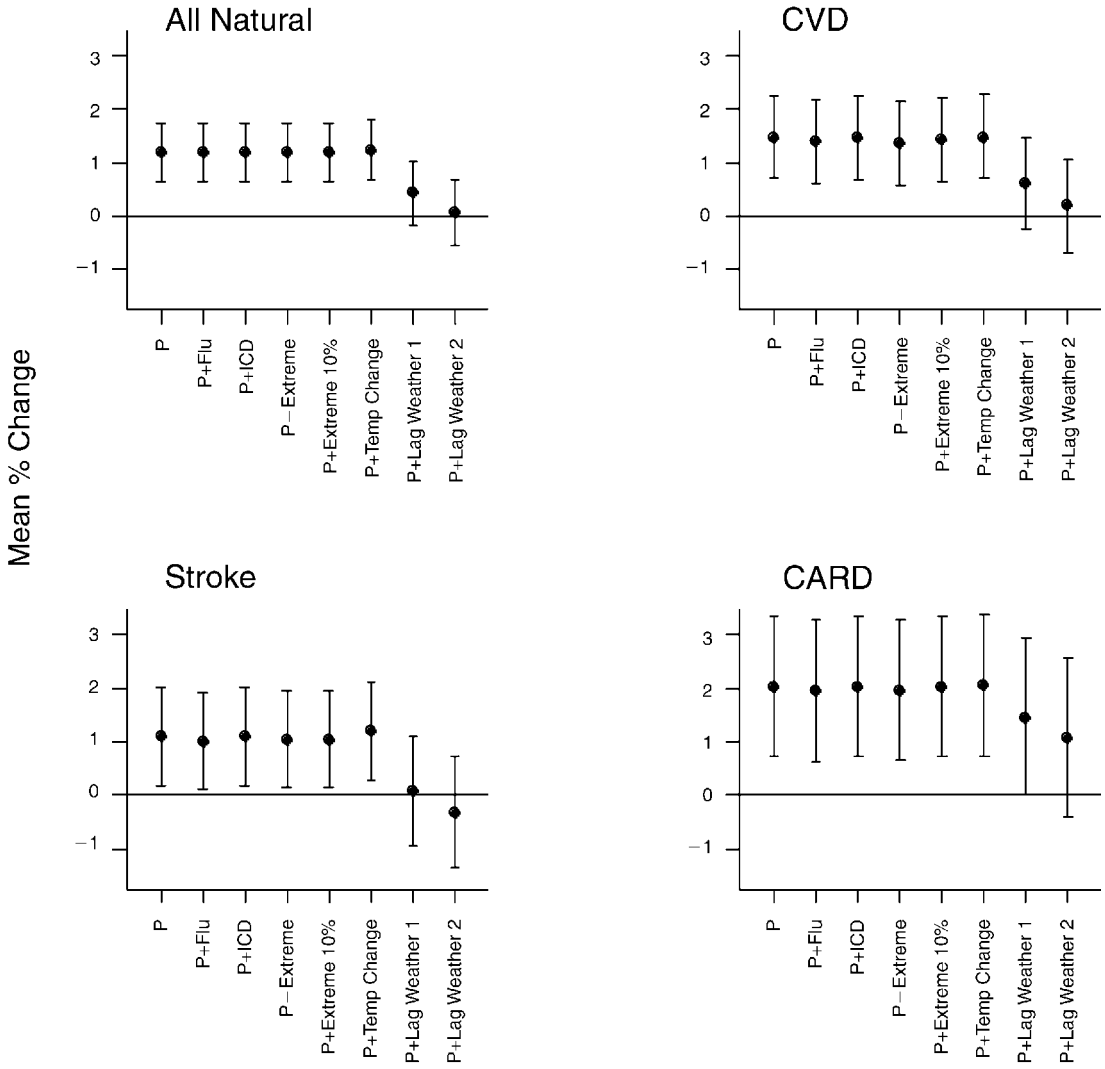

Figure 14. Sensitivity analyses for different model specifications for SO_2 at lag 0–1 day by cause of death. P indicates primary model; P+Flu indicates adding flu season; P+ICD indicates adding ICD indicator; P−Extreme indicates excluding extreme weather indicators; P+Extreme 10% indicates using extreme weather indicators based on 10th percentile; P+Temp Change indicates adding daily temperature change (high − low); P+Lag Weather 1 indicates adding lag 1–2 day mean for weather terms; and P+Lag Weather 2 indicates adding lag 1–2 day mean and lag 3–7 day mean for weather terms.

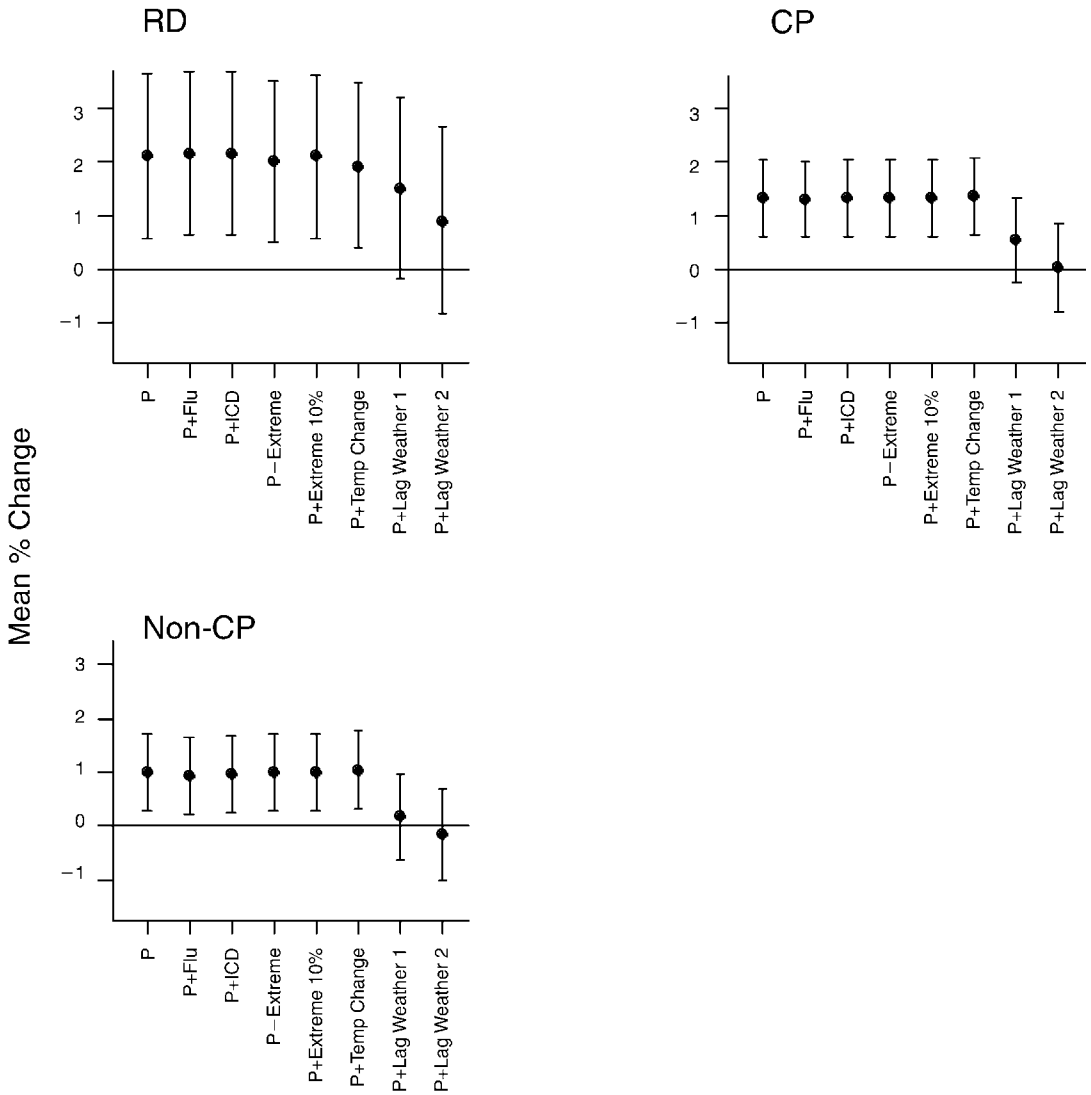

Figure 14 (*Continued*).

Table 14. Two-Pollutant Regression Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in NO_2 Concentration for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a]

Cause of Death / Pollutant(s)	Mean % Change (95% CI)
All natural	
NO_2	1.96 (1.30 to 2.62)
$NO_2 + PM_{10}$	1.69 (0.87 to 2.52)
$NO_2 + SO_2$	1.68 (0.87 to 2.50)
$NO_2 + O_3$	2.02 (1.31 to 2.73)
Cardiovascular	
NO_2	2.12 (1.18 to 3.06)
$NO_2 + PM_{10}$	1.41 (0.24 to 2.58)
$NO_2 + SO_2$	1.64 (0.50 to 2.80)
$NO_2 + O_3$	2.22 (1.23 to 3.21)
Stroke	
NO_2	2.17 (1.07 to 3.28)
$NO_2 + PM_{10}$	1.51 (0.14 to 2.89)
NO_2+ SO_2	2.11 (0.76 to 3.49)
NO_2+ O_3	2.12 (0.97 to 3.28)
Cardiac	
NO_2	2.02 (0.44 to 3.62)
$NO_2 + PM_{10}$	1.56 (−0.42 to 3.58)
$NO_2 + SO_2$	0.87 (−1.05 to 2.83)
$NO_2 + O_3$	2.38 (0.71 to 4.07)
Respiratory	
NO_2	3.69 (1.78 to 5.64)
$NO_2 + PM_{10}$	2.84 (0.46 to 5.28)
$NO_2 + SO_2$	3.30 (0.92 to 5.74)
$NO_2 + O_3$	3.83 (1.81 to 5.90)
Cardiopulmonary	
NO_2	2.17 (1.29 to 3.05)
$NO_2 + PM_{10}$	1.68 (0.60 to 2.79)
$NO_2 + SO_2$	1.85 (0.76 to 2.95)
NO_2+ O_3	2.31 (1.37 to 3.25)
Non-cardiopulmonary	
NO_2	1.66 (0.79 to 2.53)
$NO_2 + PM_{10}$	1.64 (0.54 to 2.75)
$NO_2 + SO_2$	1.46 (0.39 to 2.55)
$NO_2 + O_3$	1.74 (0.81 to 2.69)

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; and local smoothing over 2 peaks of mortality and the remaining period.

Table 15. Two-Pollutant Regression Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in SO_2 Concentration for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a]

Cause of Death / Pollutant(s)	Mean % Change (95% CI)
All natural	
SO_2	1.20 (0.66 to 1.74)
$SO_2 + PM_{10}$	0.90 (0.34 to 1.47)
$SO_2 + NO_2$	0.39 (−0.28 to 1.05)
$SO_2 + O_3$	1.13 (0.54 to 1.71)
Cardiovascular	
SO_2	1.47 (0.70 to 2.25)
$SO_2 + PM_{10}$	1.04 (0.22 to 1.86)
$SO_2 + NO_2$	0.67 (−0.28 to 1.63)
$SO_2 + O_3$	1.48 (0.68 to 2.29)
Stroke	
SO_2	1.10 (0.19 to 2.02)
$SO_2 + PM_{10}$	0.64 (−0.31 to 1.61)
$SO_2 + NO_2$	0.07 (−1.04 to 1.20)
$SO_2 + O_3$	1.03 (0.10 to 1.98)
Cardiac	
SO_2	2.04 (0.74 to 3.37)
$SO_2 + PM_{10}$	1.77 (0.39 to 3.17)
$SO_2 + NO_2$	1.61 (0.00 to 3.25)
$SO_2 + O_3$	2.43 (1.07 to 3.82)
Respiratory	
SO_2	2.10 (0.58 to 3.63)
$SO_2 + PM_{10}$	1.46 (−0.13 to 3.08)
$SO_2 + NO_2$	0.51 (−1.36 to 2.42)
$SO_2 + O_3$	1.88 (0.27 to 3.53)
Cardiopulmonary	
SO_2	1.33 (0.62 to 2.05)
$SO_2 + PM_{10}$	0.96 (0.21 to 1.71)
$SO_2 + NO_2$	0.43 (−0.45 to 1.31)
$SO_2 + O_3$	1.24 (0.47 to 2.01)
Non-cardiopulmonary	
SO_2	1.01 (0.29 to 1.73)
$SO_2 + PM_{10}$	0.80 (0.03 to 1.57)
$SO_2 + NO_2$	0.28 (−0.61 to 1.18)
$SO_2 + O_3$	1.03 (0.27 to 1.80)

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; and local smoothing over 2 peaks of mortality and the remaining period.

Table 16. Generalized Cross-Validation Statistics for Various Regression Models for NO_2 for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a]

	Regression Model						
Cause of Death	Smoothed	Linear	PW25	PW50	PW75	PW100	*P* Value[b]
All natural	1.370505	1.368172	1.368566	1.368679	1.370097	1.369977	0.098
Cardiovascular	1.315842	1.312948	1.311128	1.314569	1.313957	1.314735	0.606
Stroke	1.143113	1.140039	1.140689	1.141319	1.141774	1.141376	0.679
Cardiac	1.137656	1.137799	1.137705	1.137754	1.136988	1.138958	0.086
Respiratory	1.410495	1.404550	1.406538	1.406762	1.407474	1.406598	0.251
Cardiopulmonary	1.392155	1.388159	1.388075	1.389955	1.390153	1.390126	0.949
Non-cardiopulmonary	1.047527	1.048235	1.049730	1.045888	1.048718	1.049714	0.055

[a] The models included the base model plus different specifications of NO_2 relationship to the logarithm of cause-specific mortality (i.e., log(death) = base model + f(NO_2)). The "smoothed" model specified a smooth function for NO_2 (df = 3), and the "linear" model specified a linear function for NO_2. The piecewise regression (PW) model allowed the slope of NO_2 to change after the cutoff point at concentration x (x = 25, 50, 75, and 100 μg/m^3, respectively). The model yielding the smallest GCV value indicates the best fit.

[b] *P* value for testing whether the "smoothed" model significantly improved model fit from the "linear" model using the likelihood ratio test (df = 2).

We observed that daily mortality increased with NO_2 exposure level. Reviewing the GCV values (Table 16) and the exposure–response curves shown in Figure 15, we observed a slight alteration in the slope of NO_2 around 50 μg/m^3 for several mortality categories, around 70 μg/m^3 for CARD mortality, and around 45 μg/m^3 for non-CP mortality. However, we found such changes did not render the nonlinearity test — based on the likelihood ratio test and with the addition of quadratic terms (not shown) — statistically significant, thus suggesting the appropriateness of assuming a linear relation between daily mortality and NO_2. For SO_2, the curves show heterogeneity (Figure 16). There were observable linear exposure–response relations for all natural, CARD, CP, and non-CP mortality. The likelihood ratio test for nonlinearity of the relations was statistically insignificant, thus suggesting a linear relation (Table 17). The likelihood ratios for nonlinearity between O_3 and mortality from different causes and the exposure–response relation curves are shown in Table F.1 and Figure F.1, respectively, in Appendix F.

INTERACTION BETWEEN POLLUTANTS AND EXTREMELY HIGH TEMPERATURE

Descriptive Analysis

Descriptive statistics of the daily mean concentrations of the four pollutants and of temperature and RH in the normal, low, and high temperature periods are summarized in Table 18. The daily mean concentrations of PM_{10}, SO_2, and NO_2 were much lower on high temperature days than on low temperature days and normal temperature days. The 8-hour mean concentrations of O_3, as expected, were higher on the high temperature days than on the low temperature days and normal temperature days. There was a great difference in daily mean temperature among the three temperature groups (high: 33.1°C; normal: 18.0°C; low: 2.2°C). A small difference in daily mean RH occurred among the three temperature groups. There were considerable temporal variations in mean daily levels of pollutants (Table C.3 in Appendix C). The daily mean concentrations of SO_2 and NO_2 increased dramatically during the study period. Spatial variations in pollutant concentrations were also observed (Tables C.4–C.9). Despite these variations, we found that the distributions of PM_{10} over distances were fairly homogeneous, as shown by the high Pearson correlation coefficients (0.83–0.97) between measurements from the monitoring stations (Table C.15). SO_2 and NO_2 had a similar homogeneous distribution except during the high temperature days (Table C.17). The distribution of the daily number of deaths by cause and temperature group is shown in Table C.18 in Appendix C. There were few days with no deaths, and the 11 without deaths were all days with normal temperature. The variances were all greater than the means, indicating that mortality was overdispersed across the three temperature groups, especially for the high temperature group.

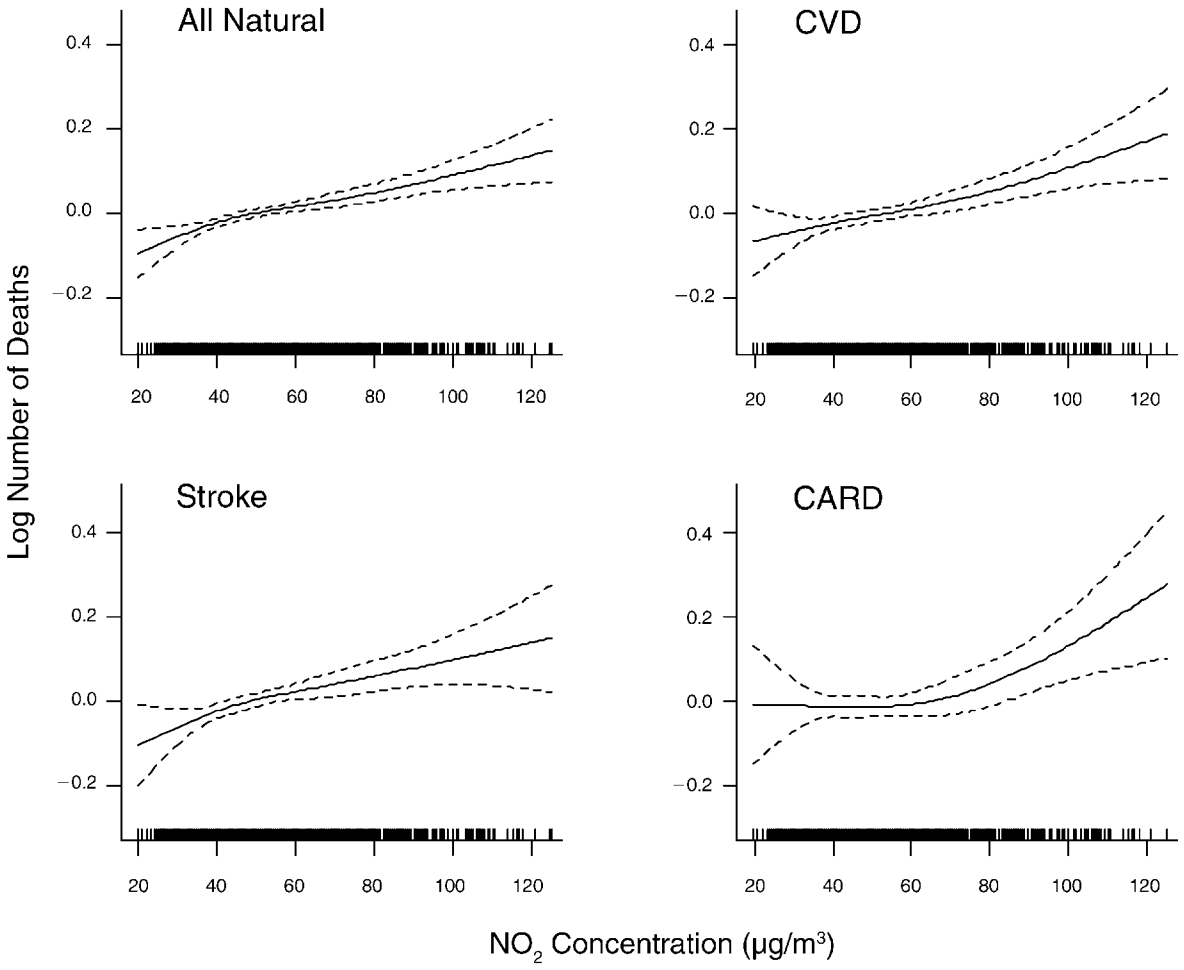

Figure 15. Exposure–response curves by cause of death for the mean percentage of change in daily mortality per 10-μg/m^3 increase in NO_2 concentration evaluated at lag 0–1 day. The solid lines represent the estimated mean percentage of change. The dotted lines represent the 95% CI.

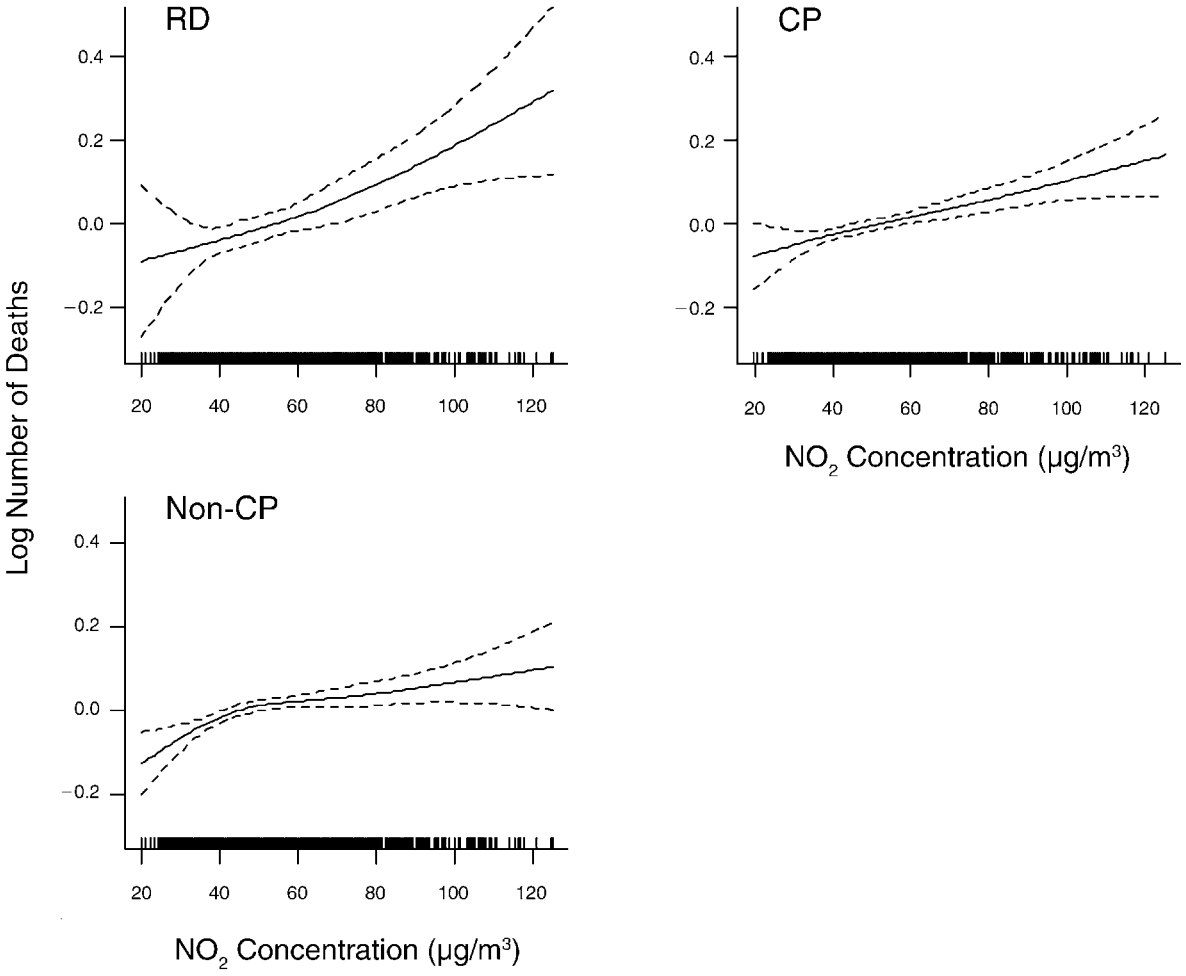

Figure 15 (*Continued*).

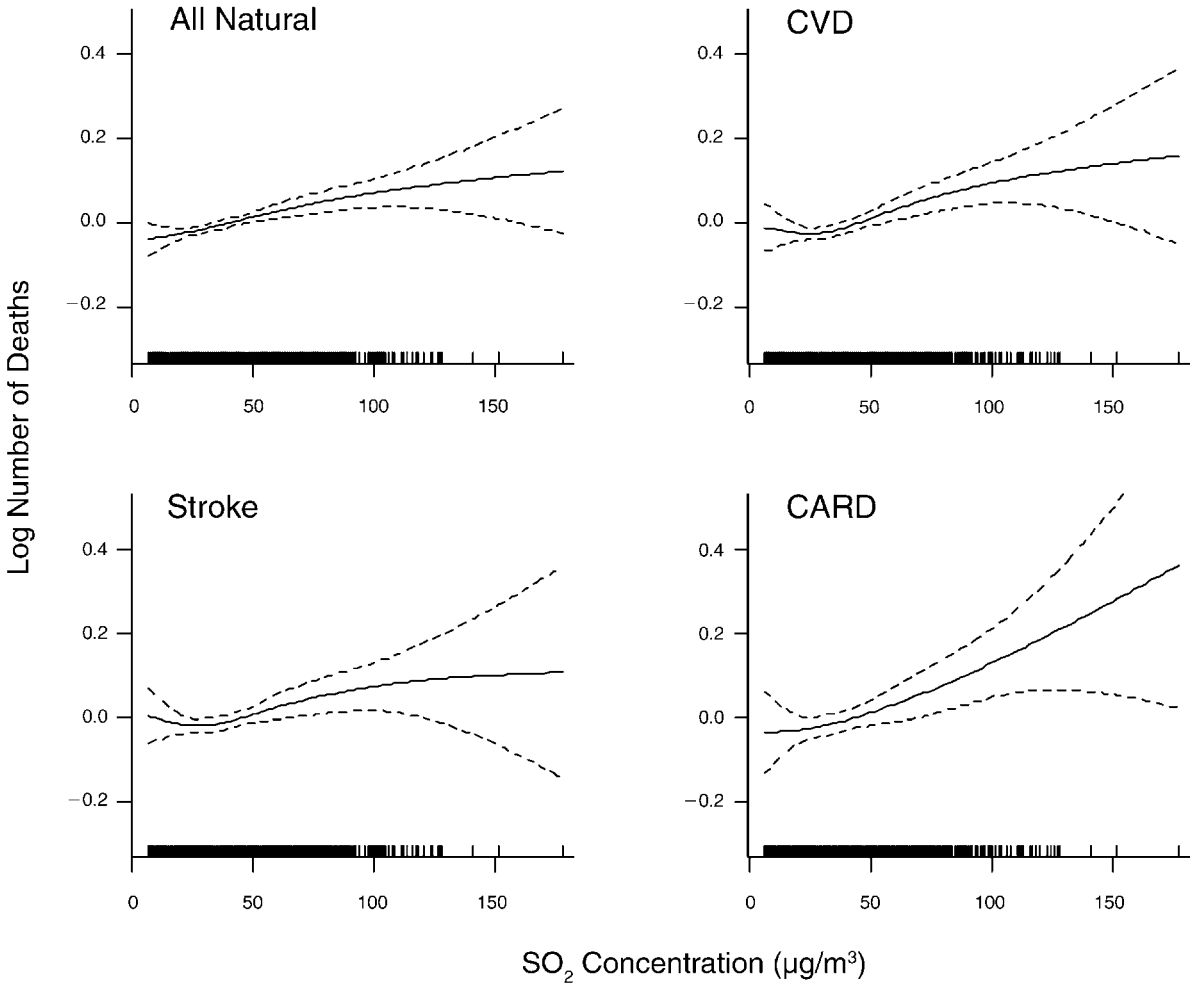

Figure 16. Exposure–response curves by cause of death for the mean percentage of change in daily mortality per 10-μg/m^3 increase in SO_2 concentration evaluated at lag 0–1 day. The solid lines represent the estimated mean percentage of change. The dotted lines represent the 95% CI.

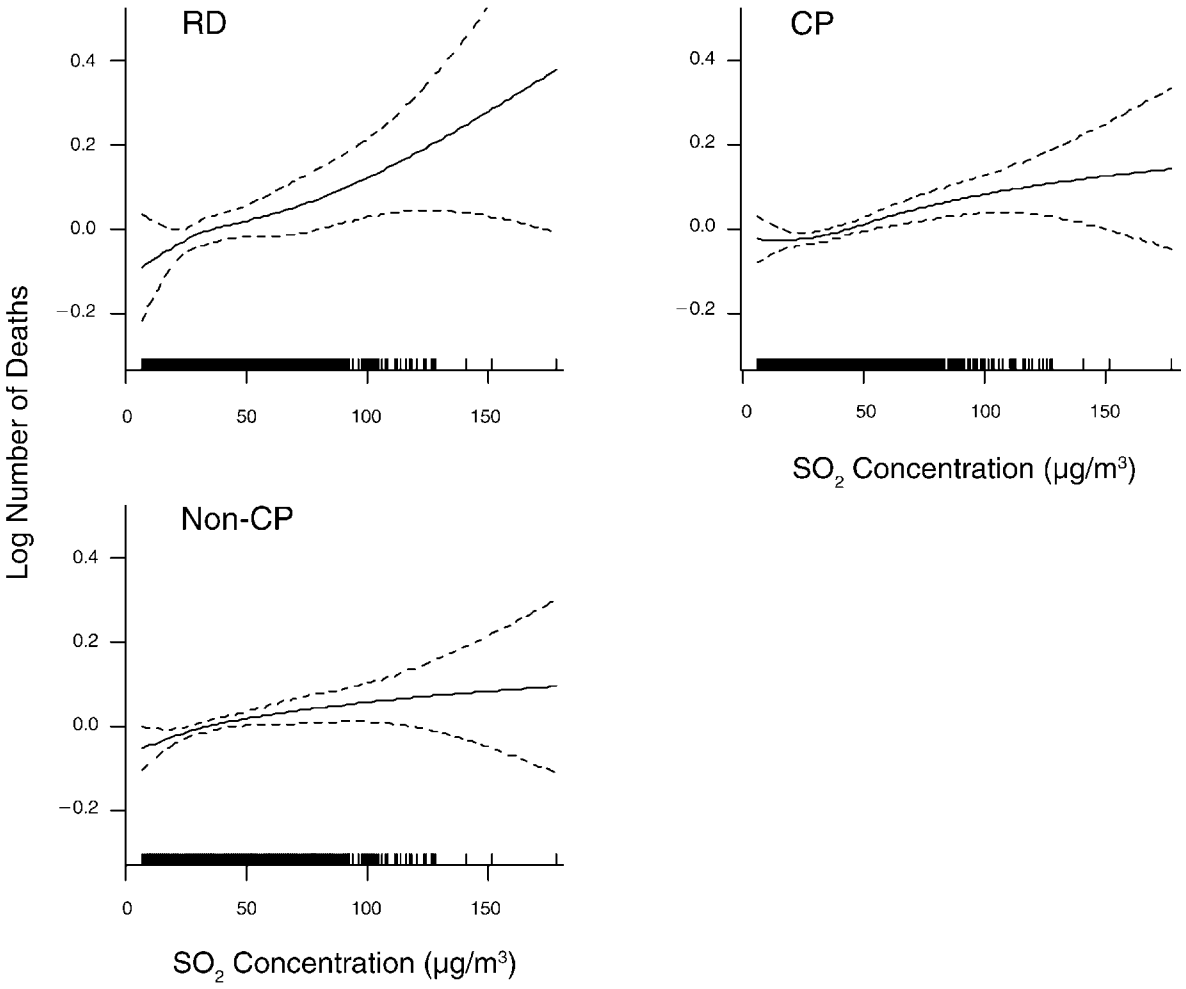

Figure 16 (*Continued*).

Table 17. Generalized Cross-Validation Statistics for Various Regression Models for SO_2 for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a]

	Regression Model								
Cause of Death	Smoothed	Linear	PW25	PW50	PW75	PW100	PW125	PW150	*P* Value[b]
All natural	1.384613	1.381436	1.383401	1.383383	1.383368	1.382812	1.383211	1.383391	0.146
Cardiovascular	1.317397	1.316602	1.317736	1.315943	1.318416	1.315902	1.316867	1.318040	0.186
Stroke	1.147774	1.146664	1.147825	1.146609	1.148279	1.147753	1.147479	1.148097	0.323
Cardiac	1.136902	1.134290	1.135802	1.134537	1.134888	1.135388	1.135775	1.135904	0.647
Respiratory	1.401886	1.398045	1.399923	1.400766	1.397353	1.396871	1.400044	1.400104	0.324
Cardiopulmonary	1.398528	1.395724	1.397305	1.397325	1.397682	1.397394	1.397026	1.397666	0.509
Non-cardiopulmonary	1.055842	1.053456	1.054359	1.053447	1.054220	1.054887	1.054748	1.054548	0.341

[a] The models included the base model plus different specifications of SO_2 relationship to the logarithm of cause-specific mortality (i.e., log(death) = base model + f(SO_2)). The "smoothed" model specified a smooth function for SO_2 (df = 3), and the "linear" model specified a linear function for SO_2. The piecewise regression (PW) model allowed the slope of SO_2 to change after the cutoff point at concentration x (x = 25, 50, 75, 100, 125, and 150 μg/m^3, respectively). The model yielding the smallest GCV value indicates the best fit.

[b] *P* value for testing whether the "smoothed" model significantly improved model fit from the "linear" model using the likelihood ratio test (df = 2).

Table 18. Distributions of Mean Daily Ambient Air Pollutant Concentrations and Weather Variables by Temperature, July 1, 2000, to June 30, 2004[a]

	Temperature					
	Normal		Low		High	
Pollutant (μg/m^3) / Weather Variable	*n* (Days)	Mean (SD)	*n* (Days)	Mean (SD)	*n* (Days)	Mean (SD)
PM_{10}	1312	145.7 (64.6)	73	117.3 (49.5)	73	96.3 (27.9)
O_3	1265	87.4 (47.5)	72	51.5 (24.5)	49	91.9 (41.8)
SO_2	1311	39.4 (25.4)	73	50.3 (26.7)	73	23.8 (10.2)
NO_2	1311	52.9 (18.7)	73	51.2 (17.8)	73	32.5 (6.2)
Daily mean temperature (°C)	1315	18.0 (8.2)	73	2.2 (1.3)	73	33.1 (0.9)
Daily mean RH (%)	1315	74.4 (12.4)	73	75.3 (16.0)	73	64.7 (5.6)

[a] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

Effect Estimates

The estimates of short-term effects by the three temperature groups for lag 0–1 day are summarized in Table 19. We observed that the interaction term of PM_{10} with temperature was statistically significant for all natural, CVD, and CP mortality, but none of the gaseous pollutants significantly interacted with temperature on mortality. Specifically, we found that the estimated effects of PM_{10} were largest on high temperature days for all natural (2.20%; 95% CI, 0.74 to 3.68), CVD (3.28%; 95% CI, 1.24 to 5.37), and CP mortality (3.02%; 95% CI, 1.03 to 5.04). The weakest effects occurred at normal temperature days, with the effects at low temperature days in the middle.

In addition to defining extremely cold days as those days whose daily average temperatures were below the 5th percentile and defining extremely hot days as those whose daily average temperatures were above the 95th percentile of the data over four years, we redefined the temperature groups using the 3rd, 7th, 10th, and 15th percentiles to examine if the effects observed in the initial analyses are similar to those found in the redefined strata. We found that the initial estimated PM_{10} effects were generally similar to

Table 19. Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in Concentration of Pollutants by Cause of Death and Temperature for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a,b]

	Temperature			
	Normal	Low	High	
Cause of Death / Pollutant	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)	*P* Value[c]
All natural				
PM_{10}	0.36 (0.17 to 0.56)	0.62 (−0.09 to 1.34)	2.20 (0.74 to 3.68)	0.014
NO_2	1.89 (1.22 to 2.57)	2.22 (0.16 to 4.32)	4.59 (−1.78 to 11.36)	0.613
SO_2	1.10 (0.55 to 1.66)	1.74 (0.25 to 3.26)	2.56 (−2.11 to 7.45)	0.505
O_3	0.19 (−0.15 to 0.54)	0.68 (−0.83 to 2.21)	1.41 (0.23 to 2.61)	0.049
Cardiovascular				
PM_{10}	0.39 (0.11 to 0.66)	0.72 (−0.25 to 1.70)	3.28 (1.24 to 5.37)	0.007
NO_2	1.89 (0.95 to 2.84)	2.03 (−0.78 to 4.92)	5.23 (−3.71 to 15.00)	0.727
SO_2	1.36 (0.57 to 2.15)	1.81 (−0.24 to 3.91)	0.35 (−6.18 to 7.32)	0.840
O_3	−0.25 (−0.72 to 0.22)	0.09 (−1.94 to 2.15)	1.39 (−0.25 to 3.06)	0.092
Stroke				
PM_{10}	0.38 (0.06 to 0.70)	0.67 (−0.50 to 1.85)	2.35 (−0.03 to 4.78)	0.222
NO_2	1.94 (0.82 to 3.06)	2.02 (−1.35 to 5.50)	4.42 (−5.96 to 15.95)	0.895
SO_2	0.99 (0.06 to 1.92)	1.32 (−1.12 to 3.82)	−0.26 (−8.01 to 8.14)	0.913
O_3	−0.27 (−0.81 to 0.28)	0.57 (−1.91 to 3.10)	1.09 (−0.77 to 2.98)	0.275
Cardiac				
PM_{10}	0.32 (−0.14 to 0.79)	0.50 (−1.10 to 2.13)	3.31 (−0.22 to 6.97)	0.229
NO_2	1.92 (0.31 to 3.55)	1.17 (−3.44 to 6.00)	−0.31 (−14.58 to 16.35)	0.911
SO_2	2.04 (0.70 to 3.39)	1.90 (−1.50 to 5.41)	−1.99 (−12.65 to 9.98)	0.771
O_3	−0.64 (−1.44 to 0.16)	−0.04 (−3.39 to 3.42)	1.45 (−1.47 to 4.46)	0.332
Respiratory				
PM_{10}	0.80 (0.25 to 1.35)	1.07 (−0.76 to 2.95)	1.15 (−3.54 to 6.07)	0.931
NO_2	3.64 (1.69 to 5.63)	3.17 (−2.13 to 8.75)	7.68 (−12.36 to 32.30)	0.896
SO_2	1.84 (0.29 to 3.41)	2.84 (−0.99 to 6.82)	12.75 (−2.59 to 30.51)	0.253
O_3	−0.06 (−1.09 to 0.99)	1.14 (−2.88 to 5.33)	2.98 (−0.79 to 6.90)	0.160
Cardiopulmonary				
PM_{10}	0.45 (0.19 to 0.70)	0.69 (−0.22 to 1.61)	3.02 (1.03 to 5.04)	0.014
NO_2	2.13 (1.24 to 3.03)	1.98 (−0.65 to 4.68)	4.31 (−4.32 to 13.72)	0.852
SO_2	1.28 (0.56 to 2.01)	1.43 (−0.46 to 3.36)	2.26 (−4.05 to 8.98)	0.930
O_3	0.04 (−0.42 to 0.50)	−0.01 (−1.89 to 1.92)	1.51 (−0.11 to 3.16)	0.123
Non-cardiopulmonary				
PM_{10}	0.27 (0.02 to 0.52)	0.33 (−0.67 to 1.34)	0.95 (−0.93 to 2.87)	0.775
NO_2	1.58 (0.69 to 2.47)	2.13 (−0.77 to 5.11)	3.27 (−4.78 to 12.00)	0.865
SO_2	0.87 (0.13 to 1.62)	1.66 (−0.46 to 3.81)	2.39 (−3.63 to 8.77)	0.670
O_3	0.22 (−0.22 to 0.66)	1.39 (−0.74 to 3.57)	0.50 (−1.01 to 2.02)	0.514

[a] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

[b] Estimates were obtained from the main effect and pollutant × temperature interaction models. The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; local smoothing over 2 peaks of mortality and the remaining period; and indicators for season.

[c] For the interaction term.

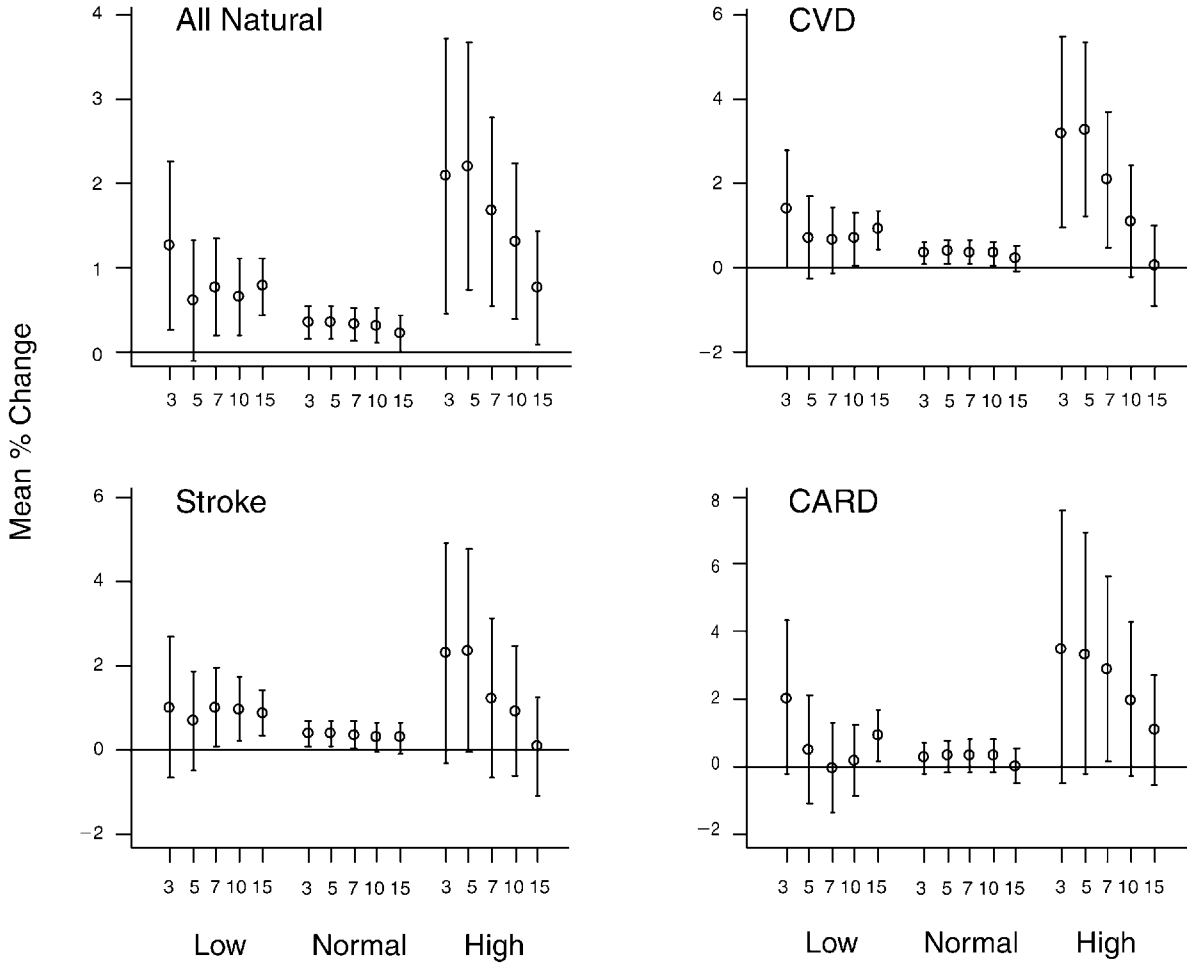

Figure 17. Mortality plots for PM_{10} by cause of death, stratified by varying percentiles of temperature cut-off points at lag 0–1 day. The labels 3, 5, 7, 10, and 15 indicate percentiles used to construct the temperature groups; "low" indicates low temperature that is < each respective percentile; "normal" indicates normal temperature that is ≥ the lower respective percentile and ≤ the upper respective percentile; and "high" indicates high temperature that is > the upper respective percentile.

the effects estimated using the 3rd percentile (Figure 17). Except for RD mortality, we observed a trend showing that the estimated PM_{10} effects decreased with the increasing percentiles across the three temperature groups, especially on the high temperature days. Figure 18 shows the main effects of temperature on mortality due to different causes stratified by PM_{10}. Given that the temperature and PM_{10} interaction existed, the results indicate positive associations between mortality and PM_{10} across the 1st, 2nd, 3rd, and 4th quartiles when the temperature was fixed. The estimated effects using the redefined temperature groups for NO_2, SO_2, and O_3 are shown in Figures E.3, E.4, and E.5 in Appendix E. Since daily temperature varies with season, a seasonal indicator was included in these data analyses. We also performed analyses without a seasonal indicator in the model, and found no significant change in the estimated effects of PM_{10} (Table E.3 in Appendix E).

With adjustment for copollutants, the significant interaction between PM_{10} and temperature remained for mortality due to all natural causes, CVD, and CP (Table 20). In the high temperature group, the largest estimates of PM_{10} effects generally remained unchanged in terms of statistically significant levels. However, adding NO_2 and SO_2 to

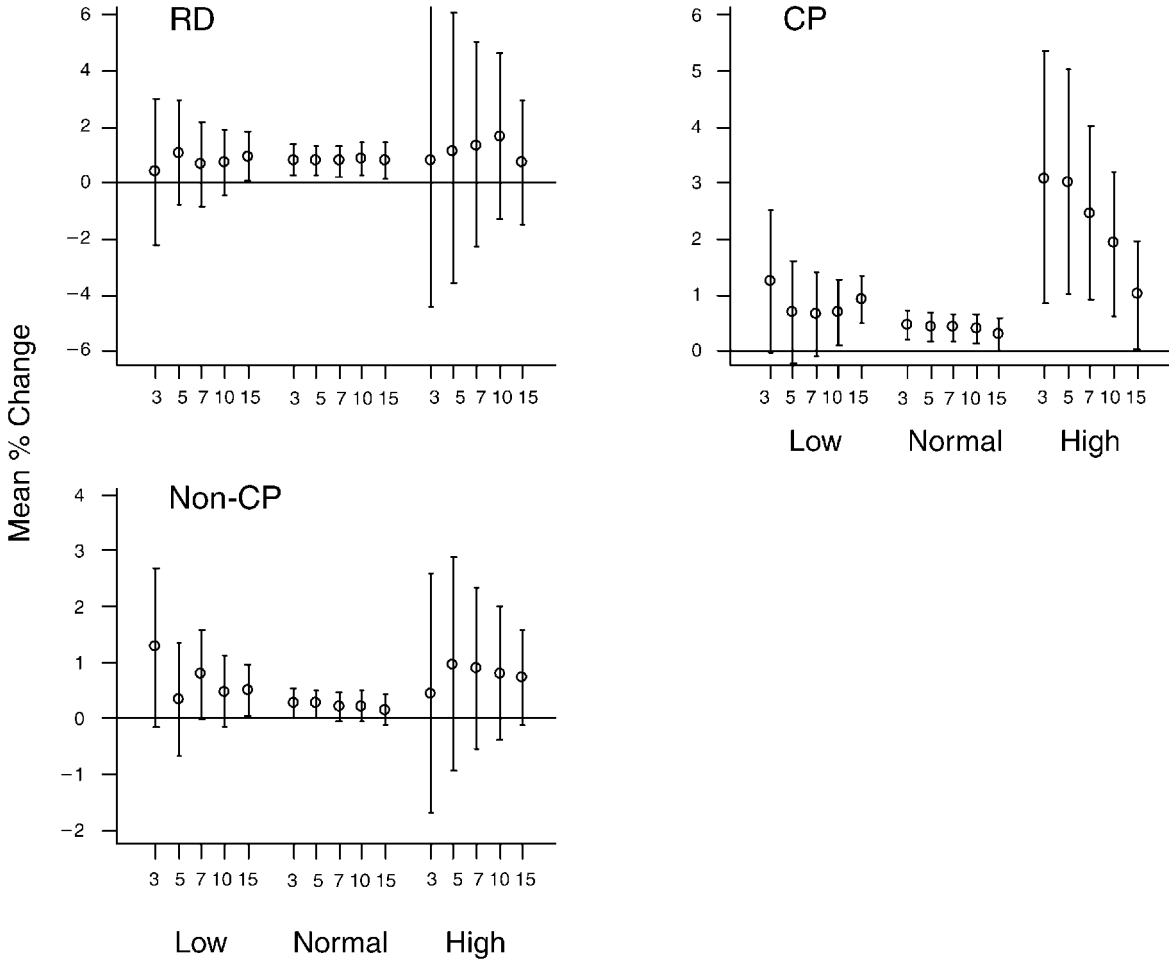

Figure 17 (*Continued*).

the models consistently reduced the estimated effects of PM_{10}. The estimated effects of NO_2, SO_2, and O_3 from the two-pollutant models are shown in Tables E.4, E.5, and E.6 in Appendix E.

UNCERTAINTY OF EFFECT ESTIMATES DUE TO CHANGE OF ICD CODE

To achieve the third aim of this study, our data analysis was extended to address the uncertainty of acute effect estimates of air pollution caused by the change in ICD coding. The method and results are detailed in Appendix G. We examined the concordance rates and kappa statistics using the mortality data from the year 2002 coded with both ICD-9 and ICD-10 codes and compared the estimated effects of air pollution. We found high concordance rates (> 99.3%) and kappa statistics close to 1.0 (> 0.98). We identified little difference in the estimated effects of air pollution on daily CVD, stroke, CARD, CP, and RD mortality (see Table G.3 in Appendix G). This study provides evidence that, based on the wide definitions of cause-specific mortality typically used in time-series studies of air pollution mortality, the change in the ICD coding does not substantially affect the estimated effects of air pollution.

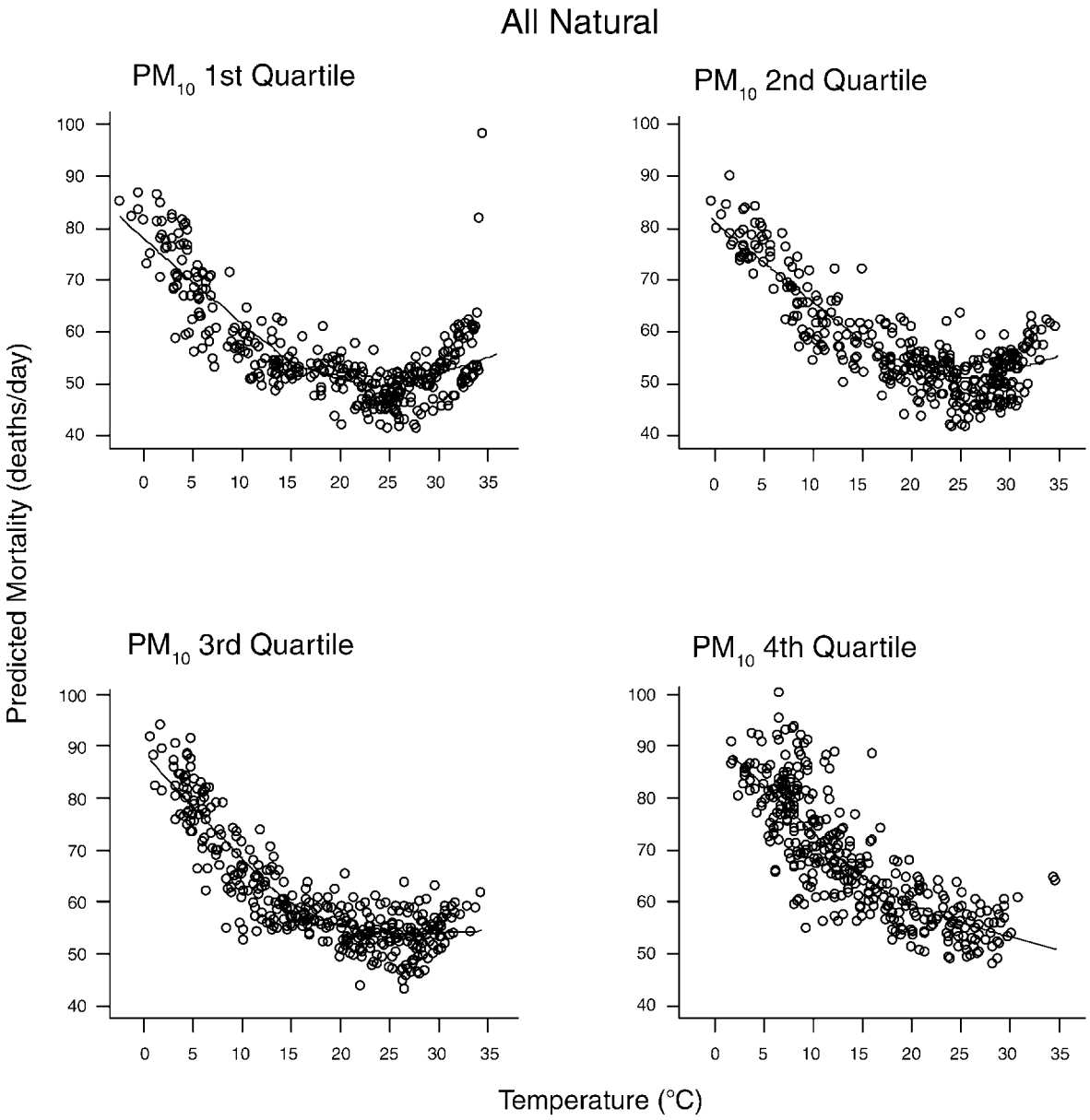

Figure 18. Main effects of temperature stratified by quartile of PM_{10} concentration and cause of death.

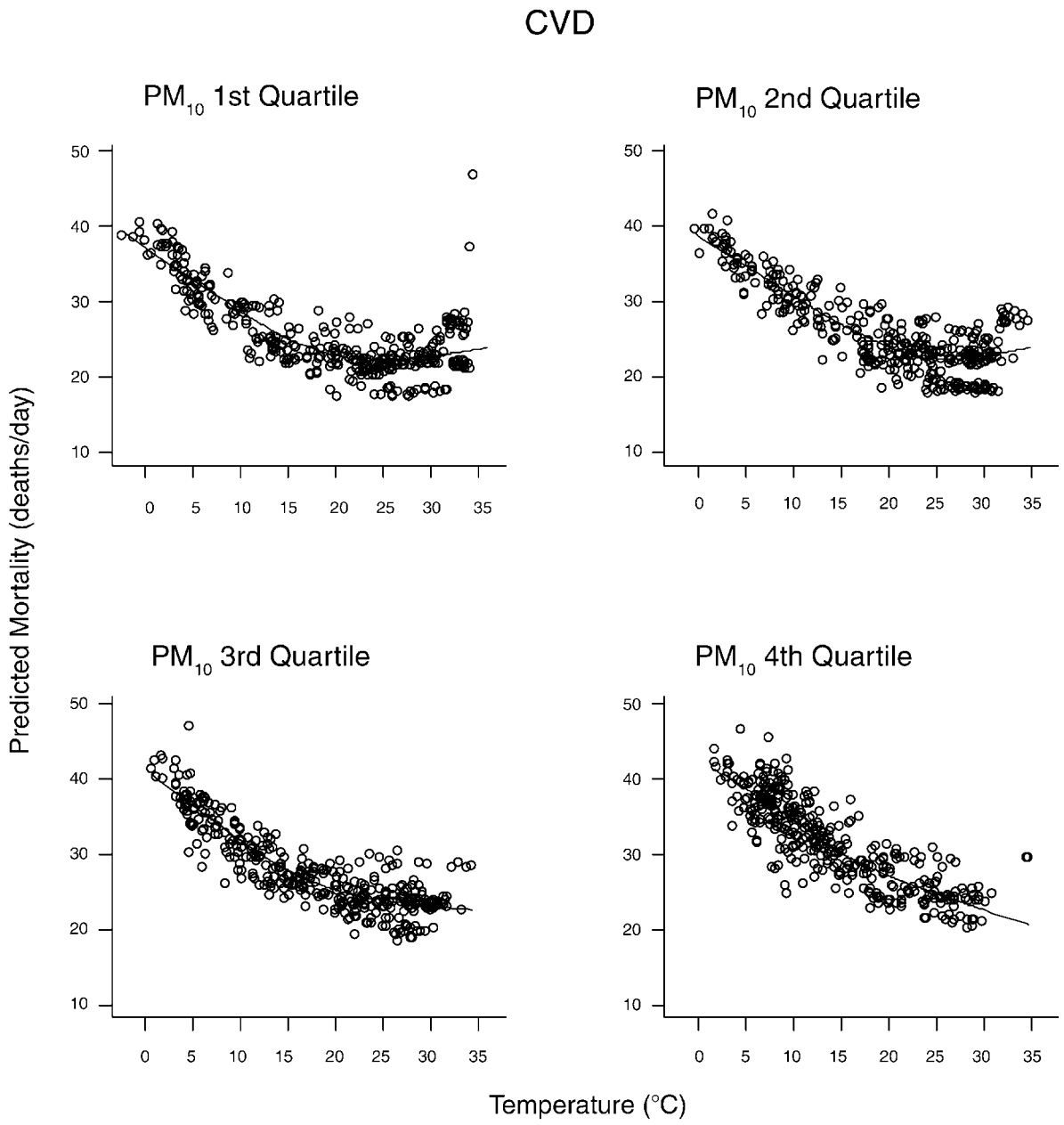

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Figure 18 (*Continued*).

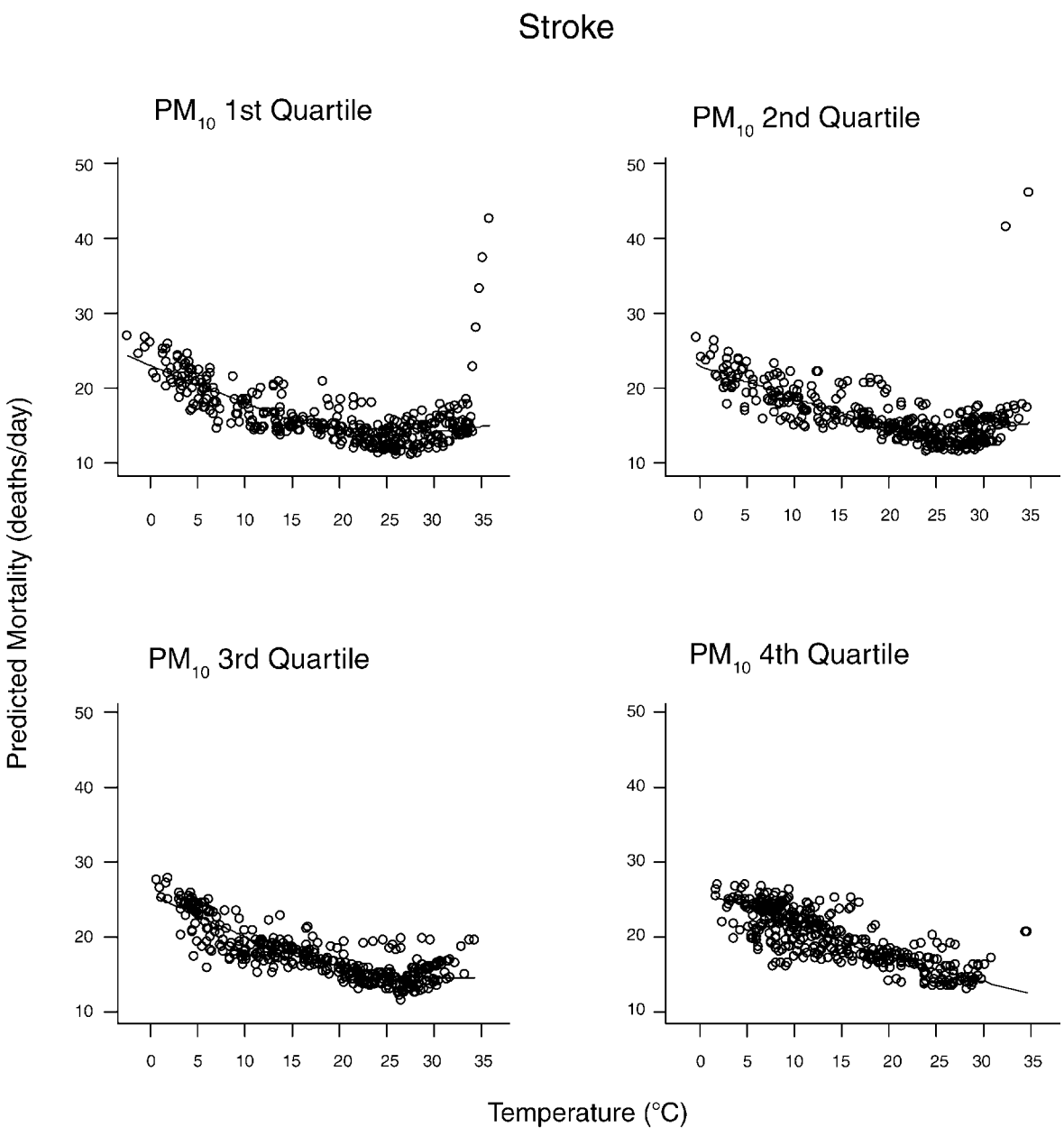
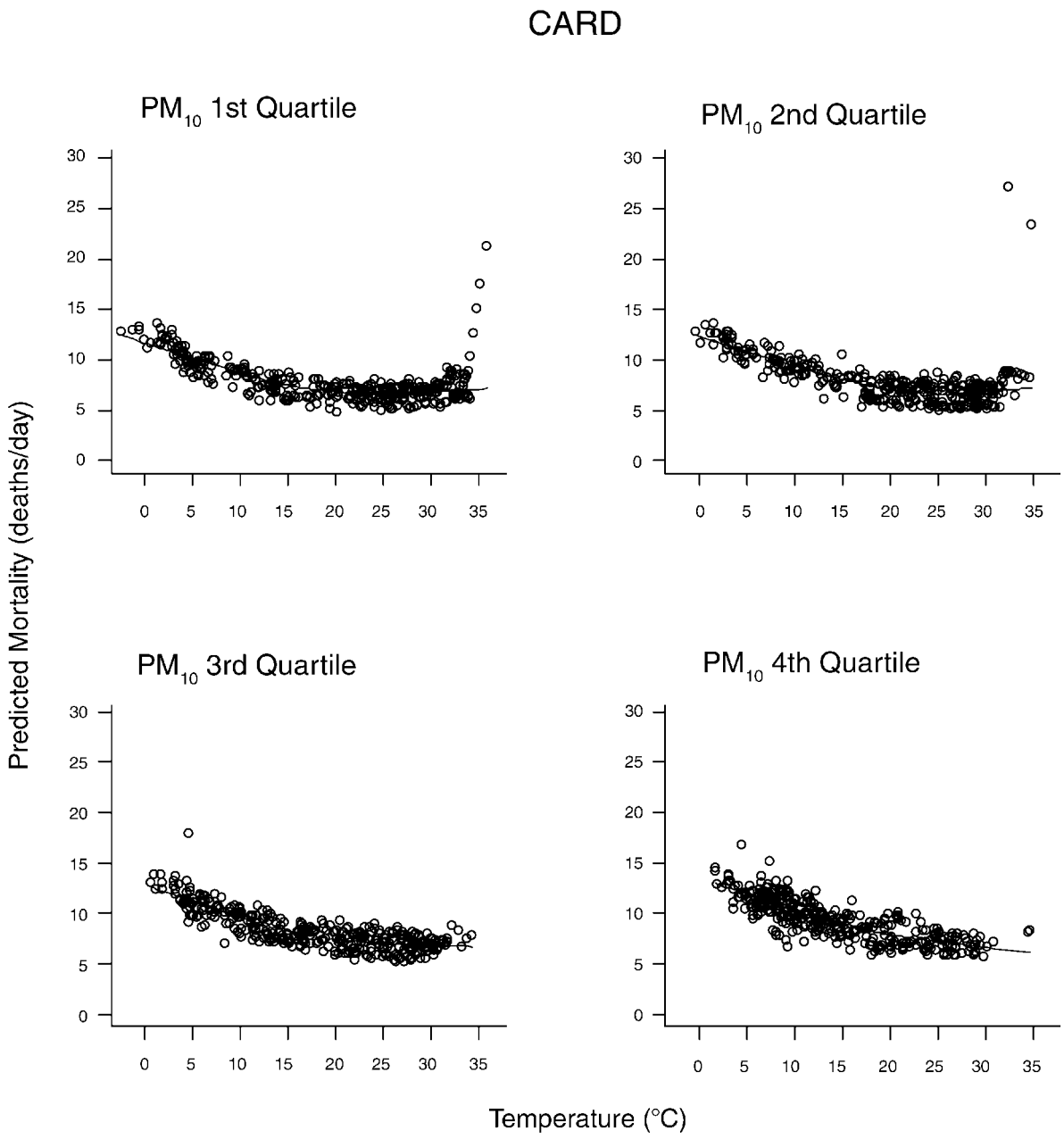


Figure 18 (*Continued*).



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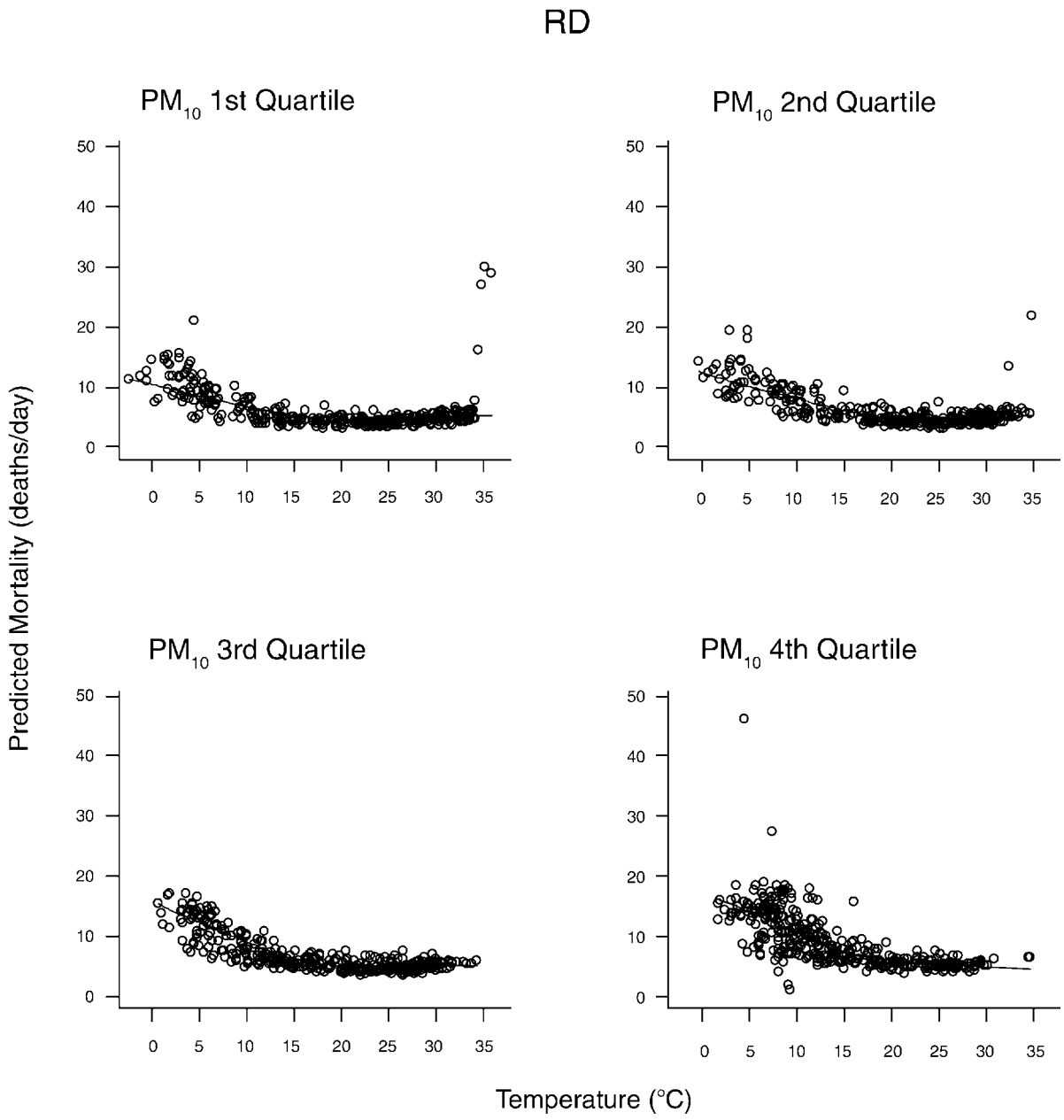

Figure 18 (*Continued*).

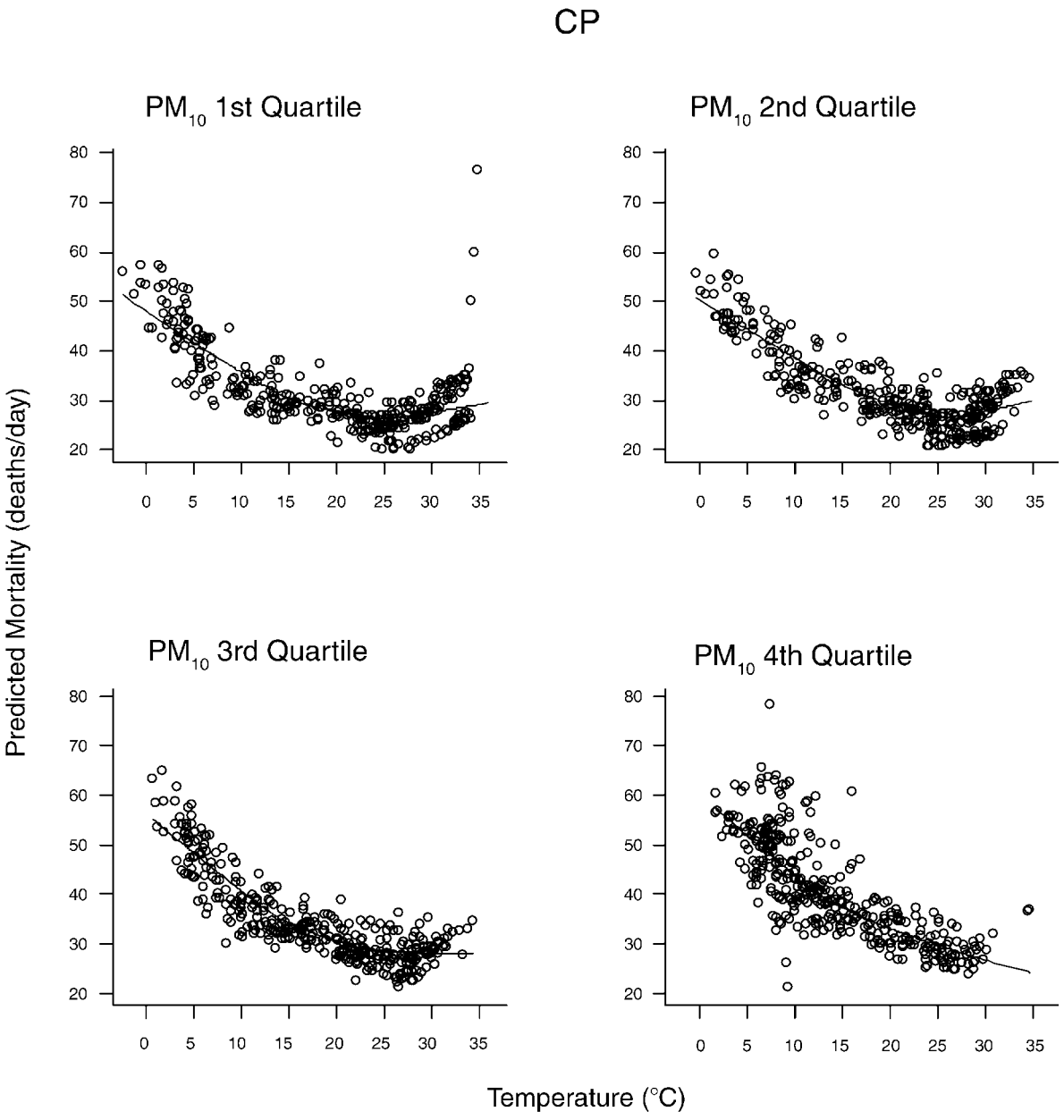

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Figure 18 (*Continued*).

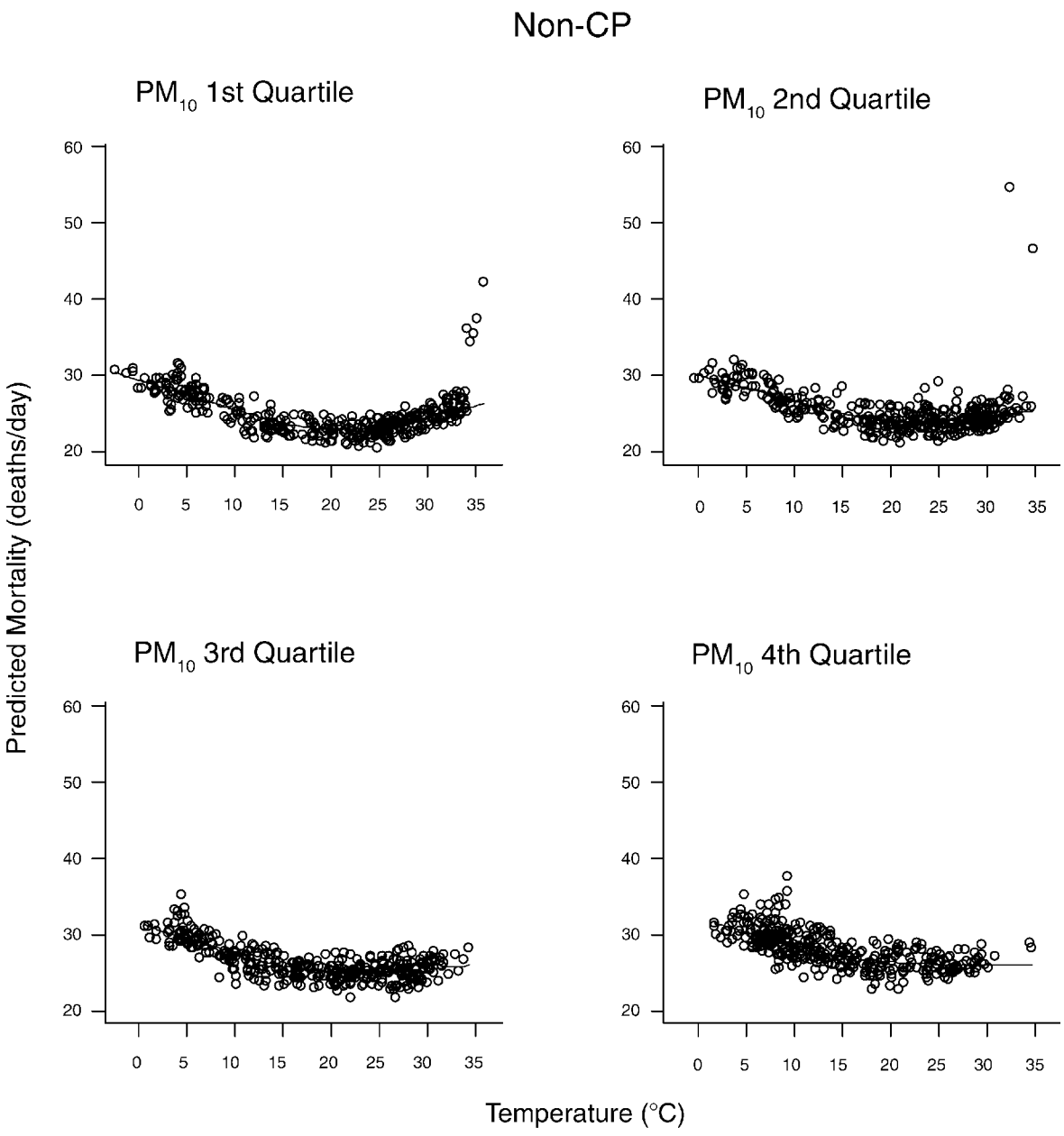

Figure 18 (*Continued*).

Table 20. Copollutant Regression Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in PM_{10} Concentration by Temperature for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a,b]

	Temperature		
	Normal	Low	High
Cause of Death / Pollutant(s)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural			
PM_{10}	0.36 (0.17 to 0.56)	0.62 (−0.09 to 1.34)	2.20 (0.74 to 3.68)
PM_{10} + NO_2	0.07 (−0.17 to 0.30)	0.24 (−0.49 to 0.97)	1.87 (0.42 to 3.35)
PM_{10} + SO_2	0.27 (0.06 to 0.47)	0.45 (−0.27 to 1.17)	2.12 (0.67 to 3.60)
PM_{10} + O_3	0.38 (0.18 to 0.58)	0.72 (0.00 to 1.44)	2.15 (0.55 to 3.77)
Cardiovascular			
PM_{10}	0.39 (0.11 to 0.66)	0.72 (−0.25 to 1.70)	3.28 (1.24 to 5.37)
PM_{10} + NO_2	0.11 (−0.23 to 0.45)	0.37 (−0.62 to 1.38)	3.00 (0.95 to 5.09)
PM_{10} + SO_2	0.27 (−0.02 to 0.55)	0.50 (−0.47 to 1.49)	3.20 (1.16 to 5.29)
PM_{10} + O_3	0.42 (0.15 to 0.70)	0.82 (−0.16 to 1.80)	3.71 (1.50 to 5.96)
Stroke			
PM_{10}	0.38 (0.06 to 0.70)	0.67 (−0.50 to 1.85)	2.35 (−0.03 to 4.78)
PM_{10} + NO_2	0.09 (−0.31 to 0.49)	0.29 (−0.90 to 1.51)	2.05 (−0.34 to 4.49)
PM_{10} + SO_2	0.31 (−0.03 to 0.64)	0.53 (−0.65 to 1.73)	2.31 (−0.07 to 4.74)
PM_{10} + O_3	0.38 (0.05 to 0.71)	0.69 (−0.48 to 1.87)	2.77 (0.25 to 5.35)
Cardiac			
PM_{10}	0.32 (−0.14 to 0.79)	0.50 (−1.10 to 2.13)	3.31 (−0.22 to 6.97)
PM_{10} + NO_2	0.02 (−0.57 to 0.60)	0.12 (−1.53 to 1.80)	3.01 (−0.54 to 6.69)
PM_{10} + SO_2	0.11 (−0.38 to 0.61)	0.14 (−1.48 to 1.78)	3.17 (−0.37 to 6.84)
PM_{10} + O_3	0.41 (−0.06 to 0.89)	0.72 (−0.90 to 2.37)	4.92 (0.96 to 9.03)
Respiratory			
PM_{10}	0.80 (0.25 to 1.35)	1.07 (−0.76 to 2.95)	1.15 (−3.54 to 6.07)
PM_{10} + NO_2	0.30 (−0.39 to 0.99)	0.44 (−1.46 to 2.36)	0.63 (−4.07 to 5.55)
PM_{10} + SO_2	0.64 (0.07 to 1.22)	0.80 (−1.05 to 2.69)	1.03 (−3.66 to 5.94)
PM_{10} + O_3	0.84 (0.28 to 1.41)	1.11 (−0.73 to 2.99)	2.66 (−2.44 to 8.02)
Cardiopulmonary			
PM_{10}	0.45 (0.19 to 0.70)	0.69 (−0.22 to 1.61)	3.02 (1.03 to 5.04)
PM_{10} + NO_2	0.15 (−0.17 to 0.47)	0.33 (−0.61 to 1.27)	2.70 (0.72 to 4.73)
PM_{10} + SO_2	0.34 (0.07 to 0.61)	0.50 (−0.42 to 1.43)	2.95 (0.96 to 4.97)
PM_{10} + O_3	0.43 (0.17 to 0.70)	0.76 (−0.16 to 1.68)	3.32 (1.16 to 5.53)
Non-cardiopulmonary			
PM_{10}	0.27 (0.02 to 0.52)	0.33 (−0.67 to 1.34)	0.95 (−0.93 to 2.87)
PM_{10} + NO_2	−0.01 (−0.33 to 0.30)	−0.04 (−1.07 to 0.99)	0.65 (−1.24 to 2.57)
PM_{10} + SO_2	0.19 (−0.08 to 0.45)	0.17 (−0.85 to 1.19)	0.89 (−0.99 to 2.81)
PM_{10} + O_3	0.31 (0.05 to 0.58)	0.49 (−0.53 to 1.52)	0.74 (−1.32 to 2.84)

[a] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

[b] Estimates were obtained from the main effect and pollutant × temperature interaction models. The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothers for time, daily mean temperature, and daily mean relative humidity; local smoothing over 2 peaks of mortality and the remaining period; and indicators for season.

DISCUSSION AND CONCLUSIONS

SUMMARY OF FINDINGS

In this time-series study in Wuhan, China, we found that short-term daily exposure to ambient air pollution was associated with daily mortality. The observed associations did not appear to be biased by the different smoothing approaches and were insensitive to different model specifications. Specifically, PM_{10} was associated with an increase in daily mortality due to all natural causes and cause-specific mortality, and the associations were particularly elevated among females and persons 65 and older. Formal examination of possible linearity in the PM_{10}–mortality relations suggests the appropriateness of assuming a no-threshold linear relation between daily mortality and PM_{10}. We also observed statistically significant interactions between PM_{10} and ex-tremely high temperature — specifically, that extremely high temperatures enhanced the effects of PM_{10} on mortality due to all natural, CVD, and CP causes. Among the gaseous pollutants, we also observed statistically significant associations of mortality with NO_2 as well as with SO_2, and the estimated effects of these two pollutants were stronger than the PM_{10} effects. The patterns of NO_2 and SO_2 associations were similar to those of PM_{10} in terms of sex, age, and linearity. Ozone was not associated with mortality from any cause.

The unique aspects of this study are as follows: First, we focused on a core city area of 201 km^2, where a high-density population (4.5 million permanent residents) has been relatively stable and homogeneous. If the suburban area had been included, the exposure measurement would not have been uniform across the study population, and we might have assigned exposures to these populations that were not representative of the true exposure. Second, in this core city area, the pollution levels are higher and the ranges are wider compared with those reported in most of the published literature. This pollution feature is ideal for exploring complicated exposure–response relations between the pollution exposure and mortality. The observed shapes of the exposure–response curves may have profound implications for developing regulations to protect public health. Third, extremely high temperatures occur every summer in Wuhan. This weather feature provided an opportunity to explore the effect modification of extremely high temperature on the association between air pollution and mortality. The observed enhanced effects of PM_{10} during the days of extremely high temperature add some new evidence to the field. Last, we assessed the uncertainty of pollution–mortality effect estimates due to the change from ICD-9-coded mortality data to ICD-10-coded mortality data. We observed that the change in the ICD coding contributed little to the effect estimates, which may be a useful reference for future similar studies.

PM_{10} Effects

Our PM_{10} findings are supported by the accumulated toxicologic data (Seaton et al. 1995; Bascom et al. 1996a,b; Fujieda et al. 1998; Nel et al. 1998). Knowledge about the respiratory actions of particles is well documented. However, an understanding of the mechanisms by which particle pollution affects CVD events is much more difficult and still lacking (Peters et al. 1997, 2001; Liao et al. 1999; Seaton et al. 1999; Brown et al. 2001). The PM_{10} findings are consistent with those of other published studies in Asia (Xu et al. 1994; Lee et al. 2000; Wong et al. 2001, 2002; Tsai et al. 2003), Europe (Anderson et al. 1996; Zmirou et al. 1998; Wichmann et al. 2000), and North America (Dockery et al. 1992; Goldberg et al. 2000, 2001, 2003; Pope III 2000; Ostro et al. 2006). Although different particle metrics were used in the previous studies, the findings all showed statistically significant and positive associations between ambient particulate air pollution and daily mortality, and suggested no-threshold linear relations between exposure and mortality. In the present study, we accounted for the joint effects of SO_2, NO_2, and O_3 in determining associations between PM_{10} and daily mortality. We found that the associations between PM_{10} and mortality were relatively unaffected in terms of statistical significance, although the magnitudes of the effects diminished after adjusting for the gaseous pollutants in the two-pollutant models. This is consistent with other studies in which weak or no confounding effects of other pollutants were observed (Morgan et al. 1998; Goldberg et al. 2000, 2003).

The magnitudes of the estimated effects of PM_{10} in this study are also similar to those from the previous studies (Goldberg et al. 2000, 2003; Ostro et al. 2006) in which a 10-$\mu g/m^3$ change in daily PM_{10} at lag 0–1 day was associated with a 0.42% increase in mortality from all natural causes. Another example is the estimated effects from the Air Pollution and Health: A European Approach (APHEA) project in Europe, which reported that mortality from all natural causes increased by 0.59% (95% CI, 0.4 to 0.8) for each 10-$\mu g/m^3$ increase in PM_{10} depending on what type of spline was used (Brunekreef and Holgate 2002). In the United States, the National Mortality, Morbidity and Air Pollution Studies (NMMAPS) reported that mortality from all natural causes increased by 0.5% (95% CI, 0.1 to 0.9) for each 10 $\mu g/m^3$ of PM_{10} (Samet et al. 2000).

It is worthwhile to note that the pollution levels were much higher in this study than in the previous studies, although the magnitudes of the effects estimates (percent change) per 10 $\mu g/cm^3$ were similar. Our explanation is as

follows: First, exposure misclassification is a major limitation of environmental epidemiologic research and is clearly applicable to this study. In this study, we assigned daily mean concentrations measured at multiple fixed monitoring stations to subjects as surrogates of their exposure. Exposure measurement errors resulting from the differences between the average exposure of the population to pollutants and the ambient concentrations of pollutants are inevitable. This misclassification of exposure belongs to the Berkson-type error and is nondifferential with respect to the population at risk, which is likely to cause a bias toward the null and lead to an underestimation of associations (Katsouyanni et al. 1997; Armstrong 1998).

Second, we speculate that differences in particle components between this study and previous studies outside Asia may have played a role. The chemical and physical processes in the atmosphere leading to the formation of particulate air pollution are potentially different. For example, our previous studies in Wuhan reported that 26%, 54%, and 17% of total ambient air particles came from natural dust, coal combustion for domestic industrial use, and automobile exhaust (He et al. 1999). In European and North American cities, automobile exhaust contributed more to ambient particle concentrations than the 17% contribution observed in Wuhan. The results of chemical analyses and toxicologic and epidemiologic studies show that particles from automobile exhaust, especially from diesel combustion engines, contain much higher concentrations of toxic species and could produce more serious health effects. A further investigation into the ambient air particle species may provide better insight into the differences reported from the various studies.

Third, ambient measurements may represent total exposure differently in Wuhan compared with Western communities. For example, a larger penetration factor (outdoor-to-indoor transport) may be expected because of the lower prevalence of air conditioning and the higher frequency of windows being open in Wuhan. Last, Wuhan residents may be less susceptible to ambient pollution, possibly due to innate differences or to such factors as differences in diet and exercise. For example, Wuhan residents walk or bicycle much longer distances in their daily lives than people in developed countries because private vehicles are limited and the bicycle is the most common mode of personal transportation. In addition, fresh vegetables are available daily to Wuhan residents. Vitamin C in vegetables is effective in counteracting air pollution effects due to its antioxidant function (Brunekreef and Holgate 2002).

Gaseous Pollutant Effects

The association of gaseous pollutants in Asia with daily mortality is more controversial than the previously reported daily mortality effects of particles. Due to a lack of pollution data, only a limited number of air pollution mortality studies have been reported in China. Xu and colleagues (1994) reported in Beijing that the total risk of mortality and the risks of mortality due to chronic obstructive pulmonary disease, pulmonary heart disease, and CVD were estimated to increase by 11%, 29%, 19%, and 11%, respectively, with each doubling in SO_2 concentration. In the Shenyang study, Xu and associates (2000) reported the estimated risks of mortality due to all natural causes and to chronic obstructive pulmonary disease increased by 2.4% and 7.4%, respectively, with a 100-$\mu g/m^3$ increase in SO_2 daily concentration; however, CVD mortality was not statistically associated with SO_2. In Hong Kong, Wong and coworkers (2001) showed that SO_2, NO_2, and O_3 were all statistically significantly associated with mortality due to all natural, CVD, and RD causes. A recent study conducted in Taipei, however, reported no statistically significant associations between the study's gaseous pollutants (SO_2, NO_2, and O_3) and mortality due to RD and circulatory disease (Yang et al. 2004). The authors concluded that the lower concentrations of air pollutants might be the reason for these nonsignificant effects.

NO_2

The observed effects of NO_2 on mortality in this study are consistent with those in previous Canadian studies (Burnett et al. 1998, 2000; Burnett et al. 2004). Similarly, Stieb and colleagues (2002) examined more than 100 time-series studies worldwide and found that estimated NO_2 effects were stronger than those of PM, O_3, SO_2, and CO. In individual studies, Kinney and Ozkaynak (1991) reported in Los Angeles County a positive and nearly statistically significant association between NO_2 and mortality. Morgan and coworkers (1998) in Sydney, Australia, also reported that NO_2 was strongly associated with mortality due to RD and that the association was independent of the effects of the other study pollutants. The authors speculated that reduced NO_2 effects on mortality due to all natural causes in the multi-pollutant compared with the single-pollutant models may be because NO_2 acts as a proxy measure for particles. In contrast to these findings, Zmirou and coworkers (1998) found that NO_2 was not consistently associated with mortality but that maximum hourly values were associated with CVD mortality in 10 large European cities after adjusting for time trend, season, influenza epidemics, and meteorologic influences.

SO_2

Sulfur dioxide was often found to be associated with mortality in western European cities (Anderson et al. 1996), but this association was not generally replicated in U.S.

studies (Dockery et al. 1992). Zmirou and coworkers (1998) studied the short-term effects of air pollution on cause-specific mortality in 10 large APHEA cities. Excess daily CVD and RD mortality was statistically significantly associated with an increase in SO_2 concentration in some western European cities, but only weakly associated with SO_2 in central European cities despite their higher air pollution levels. However, Dockery and colleagues (1992) did not find a significant association between SO_2 and daily mortality in St. Louis, Missouri, and eastern Tennessee. Although Schwartz and Dockery (1992) observed a statistically significant relation between mortality and SO_2 in Steubenville, Ohio, and in Philadelphia, Pennsylvania, the association was not independent of total suspended particles.

In the present study, we did find statistically significant associations between SO_2 and daily mortality. Nevertheless, attention should be paid to the interpretation of this association. The significant SO_2 effects were obtained with the exclusion of an important local pollution source (a smelter in the Wugang district). These effects disappeared when the SO_2 concentrations measured at the Wugang monitoring station (station 4) were included in the analyses (results not shown). The SO_2 concentrations (excluding the Wugang monitor) ranged from 5.3 to 188 $\mu g/m^3$ and were much higher than the concentrations in the U.S. cities studied in the literature. The heterogeneity of monitor-specific SO_2 concentrations in this study may cause measurement errors in the exposure assessment at the population level, which may lead to a bias toward the null hypothesis.

O_3

The association between O_3 and daily mortality has been investigated in only a few studies, and the findings have been inconsistent. Zmirou and associates (1998) showed that O_3 was associated with cause-specific and total mortality in the APHEA cities. Goldberg and coworkers (2001) found that an increase in the 3-day running mean of O_3 at a 21.3-$\mu g/m^3$ concentration was associated with deaths from all natural causes (3.3%; 95% CI, 1.7 to 5.0), cancer (3.9%; 95% CI, 1.0 to 6.91), CVD (2.5%; 95% CI, 0.2 to 5.0), and RD (6.6%, 95% CI, 1.8 to 11.8) in Montreal, Quebec, during the warm season, after adjusting for seasonal and subseasonal fluctuations in the mortality time series and the non–Poisson dispersion of the weather variables. A recent study by Zhang and coworkers (2006) reported that O_3 has stronger effects on mortality in the cold season than in the warm season in Shanghai, China. Another recent study (Bell et al. 2004) reported that an increase of 10 parts per billion in the previous week's O_3 concentration was associated with a 0.52% increase in daily mortality (95% posterior interval, 0.27% to 0.77%) and a 0.64% increase in CVD and RD mortality (95% posterior interval, 0.31% to 0.98%). However, the results were not in agreement with those reported from Lyon, France (Zmirou et al. 1996), Mexico City, Mexico (Borja-Aburto et al. 1997), or Paris, France (Dab et al. 1996), where the investigators did not observe statistically significant associations between O_3 and mortality.

We found no association between O_3 and daily mortality. However, interpretation of this finding requires caution. First, compared with PM and other gaseous pollutants, O_3 has larger spatial variations within an urban area because it can be easily "titrated" by nitrogen oxide (NO). Unfortunately, this study had measurements from only one station for estimating O_3 exposure. During the season when O_3 concentrations are low, day-to-day variation is very small, limiting the power of a time-series analysis based on daily measurements of pollutants and mortality. Second, O_3 concentrations were highly correlated with temperature. The synergistic effect between particulate air pollution and extremely high temperature on mortality found in the present study might mask an independent O_3 effect on mortality. Last, there may be large measurement errors in estimating O_3 exposure for the study population because only one O_3 monitor generated complete data in this study, and the calculated 8-hour O_3 concentration may be a poor exposure metric for the study population. Limited O_3 data (resulting from only one O_3 monitoring station) would compound any exposure measurement errors in this study. The measurement errors might lead to a bias toward the null (Katsouyanni et al. 1997; Armstrong 1998).

TEMPERATURE-MODIFIED ASSOCIATIONS

While the independent impacts of high temperatures and air pollution on daily mortality have been widely reported recently (Keatinge et al. 2000; Patz and Khaliq 2002; Staropoli 2002; O'Neill et al. 2003; Stafoggia et al. 2006; Tertre et al. 2006), few studies have investigated the potential effect of interaction between high temperature and ambient air pollution on daily mortality, and the mechanism of any synergistic effects is not currently understood (Easterling et al. 2000; Flynn et al. 2005).

Katsouyanni and colleagues (1993) did report a statistically significant interaction in Athens, Greece, on the total number of deaths between SO_2 and high temperature ($P < 0.05$) but no significant interaction between O_3 and high temperature ($P < 0.20$), while controlling for the day of the week, month, long-term trends, and holidays. It is worthwhile to note the differences between the Athens study and the current study: the daily mean temperature in July was 27.1°C in Athens, but in Wuhan it was 33.1°C during the high-temperature period; the maximum daily temperature was never above 42°C in Athens, but in Wuhan, a temperature above 40°C is historically not an uncommon

condition in summer; the ambient air pollution levels, although not directly comparable, were higher in Wuhan than in Athens (Waldman et al. 1991; Katsouyanni et al. 1993; Qian et al. 2001); and only the total number of deaths was studied in the Athens investigation.

Samet and associates (1998) developed several approaches for controlling for weather variables, including temperature, in order to estimate the independent effects of air pollution on mortality using data from Philadelphia, Pennsylvania, from 1973 to 1980. The investigators did not find any statistically significant evidence that weather variables modified the pollution–mortality relation. In a more recently published study (Koken et al. 2003) designed to determine if exposures to higher temperatures and air pollutant concentrations were significantly associated with hospital admissions for CVD in Denver, Colorado, investigators observed statistically significant pollution effects. This suggested that higher temperatures are an important factor in increasing the frequency of hospitalization for acute myocardial infarction and congestive heart failure.

Designing a study to investigate the synergistic effects of air pollution and high air temperature on mortality is a difficult undertaking because a suitable study site with both high ambient air pollution levels and extremely high temperatures is not easily available. The study city of Wuhan provides an opportunity to examine these synergistic effects. Ambient air pollution in Wuhan is a serious environmental problem, which has caused great public concern. Previous studies have shown that high concentrations of ambient $PM_{2.5}$, $PM_{10–2.5}$, PM_{10}, SO_2, and NO_2 have existed in Wuhan with concentration ranges wider than those from other cities reported in the published literature (Waldman et al. 1991; Qian et al. 2001). Studies of the long-term health effects of air pollution on the residents of Wuhan have consistently shown increased occurrences of respiratory symptoms and diseases in children and adults and decreased lung function in children living in the urban core districts (He et al. 1993; Qian et al. 2000). However, the short-term mortality effects have not been examined in Wuhan. The present study found that the interaction between PM_{10} concentrations and mortality due to all natural causes and cause-specific mortality was statistically significant ($P < 0.05$), showing mortality effects from PM_{10} enhanced by extremely high temperatures, even though daily concentrations of PM_{10} were lower on days of extremely high temperature. It is worth noting that the residual confounding by temperature cannot be excluded completely in this study as indicated by wide CIs (Table 19), as well as strong temperature–mortality associations (Figure 18).

We speculate that the following environmental features are related to the statistically significant synergistic effects of PM_{10} and extremely high temperature. First, the maximum temperature often exceeds 40°C and lasts about 2 weeks in Wuhan for most summers. Wuhan's special topography produces narrow differences in daily maximum and minimum temperatures. Even around midnight in the summer, an air temperature inside a residence above 32°C is not uncommon. Thus, Wuhan residents were exposed to extremely high temperatures for a longer period of time than those living in many other cities (Keatinge et al. 2000). Second, few of the residences in Wuhan were built with energy conservation in mind so that a vast amount of radiant energy could easily infiltrate buildings directly and be absorbed even when all of the windows were closed. The temperature inside was commonly comparable to the temperature in the shade outside. In addition, air conditioners have seldom been used because of the high cost of electricity. Third, the most common means of cooling is the use of fans, which may be effective in protecting against heat stress in areas with less extreme high temperatures. However, with the extremely high temperature in Wuhan, the use of fans could increase the level of heat stress by aggravating dehydration. The U.S. Centers for Disease Control and Prevention has stated that fans are not protective at temperatures above 32.3°C with RH above 35% (U.S. CDC 1995). Last, the high population density in Wuhan adds to the urban heat "island effect," meaning that the temperature is somewhat higher in the urban core areas than in the suburban areas, primarily because of the abundance of heat-retaining surfaces such as concrete and black asphalt.

Unlike the other study populations in the published literature, the residents in Wuhan are believed to be better adapted to extremely high temperatures because of the perennially hot summer climate (Qian et al. 2008). Heat-related mortality is more likely to occur in areas where extreme heat occurs infrequently because hypothetically those populations are less adapted to high temperatures (Kalkstein 2000; O'Neill et al. 2003). Therefore, the high pollution levels in Wuhan might play a more important role than high temperatures in the observed synergistic effects.

In this study, we found PM_{10}-associated higher excess risk for daily mortality for persons $\geq$ 65 years. Flynn and colleagues (2005) observed that many of the elderly people who died in the heat wave in France in 2003 were dehydrated, hypernatremic, and hyperkalemic, with evidence of renal failure. The investigators postulated that the most probable causes of death during the heat wave were the resultant thromboembolic disease and malignant cardiac arrhythmias, as well as the consequences of heat-induced sepsis-like shock (Vanhems et al. 2003). Other proposed risk factors in the elderly were as follows: First, elderly

people develop renal failure easily and are likely to have diminished renal tubular conservation of sodium and water during periods of dehydration (Flynn et al. 2005). Second, elderly people tend to be unable to obtain sufficient volumes of water because thermal and thirst sensitivity decreases with advancing age, especially with extremely high temperatures (Keatinge et al. 1986; Kumar and Berl 1998). The reduced thermoregulatory responses in the elderly may blunt thermoregulatory behavior during heat stress and thus are likely to cause hyperthermia or hypothermia, which may in turn aggravate other CVD risk factors and trigger events (Natsume et al. 1992). And, third, hyperkalemia is likely to occur in dehydrated, frail, elderly people because of the diminished fluid absorption even in the absence of renal disease, which can potentially lead to fatal cardiac rhythm disturbances (Flynn et al. 2005).

STUDY LIMITATIONS

Mortality Data

The mortality data were obtained from secondary electronic data sets deposited in the WCDC. The key assumption in using these mortality data was that they were sufficiently accurate and stable over time to define the underlying cause of death. However, previous studies reported that the accuracy of coding varied with cause of death, especially when the deceased had more than one condition concurrently and more than one contributed to death (Engel et al. 1980). No data were available on the accuracy of reported underlying causes of death in Wuhan. The coding process is complicated by the difficulties of determining one underlying cause of death in a complex chain of health conditions (Goldberg and Burnett 2003). Misclassification of the underlying cause of death may occur.

We used three approaches to minimize any potential misclassification in this study. First, during the study design phase, we chose a relatively wide range of categories of cause of death in order to avoid potentially serious misclassification of cause-specific mortality. This approach is expected to reduce misclassification of the underlying cause of death caused by the change from ICD-9 to ICD-10 coding. Second, from the WCDC staff, we ascertained that they had not switched from manual to computerized recording of data during the time period of the study, thus avoiding any possible confusion due to change in the recording method. The WCDC was the first center in China to standardize its system for the collection of mortality data in 1992. This system was approved and recommended by the Chinese Department of Health. Strict quality assurance/quality control procedures have been applied to the whole process of data collection from the original death certificates to the final electronic data sets (see Appendix J available on the HEI Web site). Last, an independent audit was done in conjunction with HEI (see Appendix H).

In order to explore whether the change from ICD-9- to ICD-10-coded mortality data might produce misclassification of cause-specific mortality and potentially affect the pollution–mortality relations, we conducted an additional analysis focusing on only one year of mortality data to identify any potential difference due to the shift in ICD coding in estimates of the mortality effects of pollution. In that analysis, we found high concordance rates between the ICD-9- and ICD-10-coded mortality data, and the maximum change in the estimated pollution mortality effect was 0.05% (for the NO_2 effect on CARD and RD mortality). The results from that analysis show little change in the effect estimates due to the shift of the coding system from ICD-9 to ICD-10.

Air Pollution Measurements

We used PM_{10}, SO_2, and NO_2 measures collected from five fixed monitoring stations and O_3 measures from one fixed monitoring station in this study. A simple average of daily concentrations across all monitors in the city was used as a surrogate of a participant's daily exposure. Although these fixed monitoring stations are all distributed within the small urban core area of 201 km^2, there may be spatial variations within the city, which would raise the question of whether the simple averages are representative of the exposure for the study population (Kunzli and Schindler 2005). We used two methods to address this question. First, we calculated a surrogate exposure variable representing a participant's daily exposure using the centering method, in addition to using the simple averaging method. We then compared the distributions of the estimated daily exposures calculated from both methods. The results show that the means, standard deviations, and 25th, 50th, and 75th percentiles are quite similar. Differences in the means of PM_{10}, NO_2, and SO_2 concentrations are all less than 1 $\mu g/m^3$ (Tables C.2 and C.3 in Appendix C). In calculating the representative exposure variables for the whole study population, we found that the similarities in the distributions support the use of either method to calculate daily mean concentrations of the pollutants studied, to be used as surrogate exposure variables in the statistical models. Furthermore, we compared the mortality effects of daily concentrations of pollutants calculated using the simple averaging method with those calculated using the centering method and found that there is little difference between them (see Table E.7 in Appendix E).

Second, correlations in the monitor-specific daily mean concentrations were high except for SO_2, indicating that the measures of the pollutants reflected the urban background level of ambient air pollution and supporting estimation of

the representative exposure variables for the whole study population through use of the daily concentrations of pollutants collected from all the monitoring stations. Very weak correlations existed between SO_2 daily concentrations measured at the Wugang monitoring station (station 4) and the concentrations measured at any of the other monitoring stations. This is because a big ferrous smelter is located in the Wugang district that consumes a large amount of coal and emits high levels of SO_2 into the air, and therefore the daily SO_2 concentrations measured at the Wugang monitoring station were higher than those at the other stations. Thus, we conducted data analyses excluding SO_2 measures collected at this heavily industrialized district in this study. As for O_3, we were limited in addressing the exposure uncertainty because there was only one O_3 monitoring station available for the study.

Association Validity

An evaluation of whether the observed associations are valid requires consideration of the role of chance, confounding, and bias as possible alternative explanations. Chance is unlikely to be a possible explanation in this study, especially for PM_{10}, NO_2, and SO_2, because the daily pollution data were almost complete for these pollutants, and there were zero days with no deaths during the four-year study period. The large sample size combined with the feature of a complete time series of the daily mortality and daily pollution data provided sufficient statistical power to detect increases in daily mortality. The fairly narrow CIs obtained indicate that the observed associations were statistically stable, including the associations estimated by stratified analyses of age, sex, and extremely high temperature.

The major potential bias in this time-series study is observational, or informational, bias. Misclassification is a potential concern in any study since some degree of inaccuracy in reporting or recording information is inevitable. In this study, misclassification might have occurred if participants were erroneously categorized with respect to either exposure or cause-specific mortality. The potential misclassification of cause-specific mortality was addressed previously. Regarding misclassification of exposure, ambient pollution levels at a given location might not reflect an individual's true exposure because factors such as personal mobility and time–activity patterns were not taken into account, and the distribution of the pollutants might be geographically heterogeneous. Even so, most people live and work in the same area in Wuhan (the nine core urban districts), and it has been well documented that ambient PM is distributed uniformly within a region and that outdoor, indoor, and personal PM exposures are highly correlated, especially for fine particles (Wallace 1996; Janssen et al. 1998). Consequently, we expect that any resulting exposure misclassification would lead to a conservative underestimation of the associations because this error generally belongs to the Berkson type and thus is nondifferential in nature, which is likely to cause a bias toward the null.

A particular concern with this time-series analysis is whether the observed associations were biased by the different smoothing approaches and different model specifications. We used a commonly accepted standard GAM procedure in this pollution–mortality study, during which a series of decisions had to be made. These decisions were not completely objective but were based on a certain degree of judgment and experience, which might bias the observed associations. Therefore, we conducted a series of sensitivity analyses. The major results show that the observed associations were unlikely to be biased by the different smoothing approaches and different model specifications.

Last, although we controlled for the two mortality peaks during the periods of July 28 to August 3, 2003, and December 1 to December 31, 2003, in regression models, this approach may not be adequate. Thus, we also conducted sensitivity analyses to compare the results using all the data with the results of analyses that excluded the data for those periods (see Table E.8 in Appendix E). We found little difference in the estimated effects.

The other concern is the potential confounding of important covariates. First, in view of the fact that the study city has extremely hot summers, and this extreme weather is associated with both high air pollution levels and increased mortality, the observed pollution–mortality associations may be confounded by the extremely high temperatures. In addition to selecting weather variables (daily mean temperature and daily mean RH) that minimized the residual variability in the mortality time series, after controlling for annual and seasonal patterns, we included extremely high temperature and extremely humid weather as variables in the models. Additional analyses were also performed with stratification by temperature. Results from this type of data analyses were generally quite stable, indicating that extreme weather was unlikely to confound the observed pollution–mortality associations.

Second, infectious disease epidemics could potentially confound the observed pollution–mortality associations, since data on infectious disease epidemics were not available for this study. However, we expect that we removed, at least partially if not fully, any such confounding by temporal filtering, since infectious disease epidemics generally follow seasonal and subseasonal weather patterns. In addition, we included an influenza season indicator in the model in the sensitivity analysis, and the results show that the estimated pollution–mortality associations were fairly stable. These results were in agreement with previously published studies that reported that adjustment for influenza

epidemics did not remove the associations (Spix et al. 1993; Anderson et al. 1996). Furthermore, infectious disease epidemics occur mostly in the fall and winter months, and the observed PM_{10} effects were enhanced on the extremely high temperature days occurring during the summer. Therefore, infectious disease epidemics should not have substantially confounded the estimates on the extremely high temperature days, although some residual confounding may have been possible.

Third, we did not have data on a number of factors known or suspected to affect mortality, namely, environmental tobacco smoke, indoor air pollution sources, and work environment. Nevertheless, this time-series study considered days rather than persons as the units of observation, and the estimated pollution effects were unlikely to have been substantially confounded by these factors because these factors do not vary with daily pollution exposure. In addition, high levels of $PM_{2.5}$, $PM_{10-2.5}$, PM_{10}, total suspended particles, SO_2, and NO_2 have existed for a long time in the study area; few residences were built with energy conservation in mind; and air conditioners have been used less commonly than in cities in developed countries with similar weather (Qian et al. 2004). Thus, high levels of the pollutants could easily infiltrate the homes (Waldman et al. 1991). Outdoor pollution may then be dominant, making the potential confounding of indoor pollution emission sources less important. Therefore, the surrogate for population exposure is likely to be valid.

Last, this study used a single-pollutant model to estimate pollution effects, and the copollutant adjustments were made only in two-pollutant models. This is because the high correlations among levels of most pollutants would have led to biased estimates of the effects if multiple copollutants were included in the model simultaneously. The exposure variables that we used are proxies for personal exposure to the pollutants being studied. Failure to fully control for potential confounding by copollutants may have led to a biased effect estimate since persons were simultaneously exposed to many air pollutants, and the associations observed in this study may be due to the combined effects of all pollutants. The single indicator of ambient PM_{10}, for example, stands for the mixture of pollutants rather than for one specific component of PM (Turpin 1999). It is well documented that the mass concentration of PM_{10} includes a wide array of potentially toxic chemical species including sulfates, nitrates, elements, water-soluble metals, carbon in the particle phase, ultra-fine particles, gas- and particle-phase organics, and combustion-source particles (Spengler et al. 1996). There also may be seasonal variations in the composition of PM in Wuhan. Therefore, it might be premature to ascribe the observed mortality effects solely to the mass concentration of ambient PM_{10}.

In summary, although we were unable to exclude the role of bias and confounding completely in this study, it is unlikely that they provide alternative explanations of the observed associations.

CONCLUSIONS

The findings from this study are consistent with our central hypothesis that daily ambient PM_{10} concentrations are associated with daily mortality from all natural causes as well as cause-specific daily mortality. The key findings from the current study are as follows:

- Daily ambient PM_{10}, NO_2, and SO_2 concentrations were significantly associated with mortality from all natural causes and cause-specific mortality. The observed effects of NO_2 and SO_2 were stronger than those of PM_{10}.
- Stronger mortality effects from PM_{10}, NO_2, and SO_2 were observed in females than in males, and among individuals aged ≥ 65.
- There was a significant effect modification from extremely high temperatures on the association between PM_{10} and daily mortality: specifically, high temperature enhanced the PM_{10} effects.
- There was a linear relation between daily mortality and PM_{10} and between daily mortality and NO_2. For SO_2 and O_3, the exposure–response relation demonstrated heterogeneity, with some curves showing a nonlinear relation.
- There was little difference in the estimates of the effects of ambient air pollution on mortality due to the shift in ICD coding from ICD-9 to ICD-10.

IMPLICATIONS OF FINDINGS

Our research, conducted in Wuhan, China, which has high ambient air pollution levels and extremely high summer temperatures, provides new information regarding the health effects of ambient air pollution on daily mortality. The study may provide an important international scientific context for U.S. studies of PM_{10}, NO_2, SO_2, and O_3, enabling an assessment of the plausibility of confirming U.S. findings in other geographic areas and of the adverse health effects that may be prevented by applying relevant environmental regulations. In addition, exploring the exposure–response curves, identifying susceptible populations, and determining any important synergistic effects of ambient air pollution and extremely high temperature

may have implications for both scientists and relevant governments in efforts to protect public health through the regulation of air pollution.

The synergistic effect of air pollution and high temperature on mortality observed in this study deserves particular attention because both high summer temperatures and high levels of ambient air pollution often occur in large metropolitan areas. Large cities such as Wuhan could experience an increase in the incidence of mortality on extremely hot days due to the combination of heat and high levels of air pollution. Therefore, there is a need for relevant governments to take a precautionary approach to cutting emissions, which is expected to substantially reduce both high urban temperature and ambient air pollutants, including greenhouse gases. Reducing fossil fuel combustion may also have important direct health benefits by preventing many deaths attributable annually to the combination of heat and air pollution (Smith 1993; Wang and Smith 1998).

FURTHER RESEARCH

The extensive and high-quality data available from the present study could readily be used in future studies. Three directions for further research are briefly outlined here.

First, identification of any potential modifying effect of poverty on pollution–mortality associations has profound implications for public health and regulation (O'Neill et al. 2003). The current data set provides detailed information on education levels for the deceased in Wuhan. Previous studies showed that education attainment can be a robust indicator of socioeconomic position, predicting income, living conditions, and occupation (Brunner 2001). Steenland and associates (2002) also reported that less-educated U.S. populations generally had higher mortality rates. Therefore, the combined effects of poverty and air pollution on mortality should be a focus of further study.

Second, further exploration of the seasonal patterns of pollution–mortality effects is worthwhile. The acute effects of ambient air pollution on mortality may exhibit a seasonal variation, possibly attributable to differences in exposure concentration, duration, and intensity. Furthermore, pollution species may vary seasonally, and confounding factors could be seasonally associated.

Last, climate change is projected to increase ambient temperature. Hence, epidemiologic studies allow us to further identify how thermal stresses may cause increased mortality, as well as how important factors such as ambient air pollution and poverty modify the associations between thermal stress and mortality.

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APPENDIX A. Statistical Methods and Data Analysis

GENERAL ANALYTIC STRATEGIES

To achieve the study aims, we first created a master analytic database by merging the mortality data with the air pollution data according to the calendar date of death. The finalized, clean analytic data set contained daily death frequencies and underlying causes of deaths; daily mean concentrations of PM_{10}, SO_2, and NO_2, and 8-hour average concentrations of O_3; and other needed meteorologic covariates such as daily mean temperature and daily mean RH. The primary objective of the data analysis was to quantify the association between daily mortality and daily mean concentrations of PM_{10}, SO_2, NO_2, and O_3, while adjusting for weather and temporal factors in the multivariable modeling. We derived an estimation of exposures to each of the above pollutants for each death event in terms of 0-day, 1-day, 2-day, 3-day, and 4-day lag concentrations, and lag 0–1 day and lag 0–3 day average concentrations before the death events. These exposure variables were developed by averaging monitor-specific daily concentrations of pollutants (using a simple averaging method). We also obtained additional individual-level information (e.g., age and sex) from death certificates and used these data only for determination of subgroups in stratified analyses.

DESCRIPTIVE ANALYSES

We generated descriptive statistics to check the validity of the variables and to identify potential outliers. We obtained percentages of valid daily pollutant measurements to assess the completeness of the data. In addition to the usual correlations among the study air pollutants, we also calculated complete monitor-to-monitor correlations within specific pollutants, pollutant-to-pollutant correlations within specific monitors, and partial correlations between pollutants averaged across monitors with seasonal correction. The partial correlations were performed in two steps. First, for any pair of pollutants, we fitted an individual pollutant-specific generalized additive model (GAM) that controlled for the same temporal and seasonal factors used in the main GAM model, which incorporated the pollutants and mortality due to all natural causes (see detailed

description later in this appendix). Then, we obtained the correlations between the paired pollutants. Finally, we examined the time series of the study air pollutants and cause-specific mortality counts in order to help develop adequate health outcome regression models in the subsequent data analyses.

REGRESSION ANALYSIS

The modeling technique used in this study was quasi–Poisson regression. Under the assumption that daily death counts follow a Poisson variate distribution with constant over- or underdispersion, we used quasi-likelihood estimation within the context of the GAM to model the natural logarithm of the expected daily death counts as a function of the predictor variables. This method accounts for the overdispersion in confidence intervals and *P* values (Zeger and Qaqish 1988; Hastie and Tibshirani 1990). The GAM replaces the linear component of the traditional model, $\Sigma X_{ij}\beta_j$ with $\Sigma f_j(X_{ij})$. It is particularly useful in a time-series analysis because the relations between air pollution levels and time and weather parameters are expected to have a complex form that is not easily fitted by a standard linear or nonlinear model. All model analyses in this study were performed with natural cubic spline models using the statistical software package R, version 2.5.0, along with foreign, version 0.8-20 and mgcv, version 1.3–24 (R Development Core Team 2007, Vienna, Austria). We also employed SAS, version 9.1.3.

The specific code for the core model for underlying health outcomes is as follows:

```
gam(CAUSE ~ POLL + factor(day_wk) + factor(factor_by) +
factor(extreme_cold) + factor(extreme_hot) +
factor(extreme_humid) +
s(dayseq,k=DF1*4+1,fx=TRUE, bs="cr") +
s(dayseq,k=DF1*4+1,fx=TRUE, bs="cr", by=smooth_other) +
s(dayseq,k=DF2+1,fx=TRUE, bs="cr", by=smooth_sum03) +
s(dayseq,k=DF3+1,fx=TRUE, bs="cr", by=smooth_win03) +
s(temp_avg,k=DF4+1,fx=TRUE, bs="cr") +
s(rh_avg,k=DF5+1,fx=TRUE, bs="cr"),
family=quasipoisson(link=log))
```

The explanations for each of the variables in this code can be found in Table A.1. The degrees of freedom (labeled DF1 through DF5) used for each cause of mortality can be found in Table 3 in the main text, which shows the best base model. Table A.2 shows the estimates of the overdispersion parameter used in our main models.

We used a chi-square test based on the difference of the deviance of the two models (with linear and smoothed pollutants), with 2 df.

The GAM analyses covered three areas. First, we controlled for potential confounding of yearly, seasonal, and subseasonal variations in the mortality time series, assuming that these variations in this mortality time series represent unmeasured covariates, including potential confounders of the association between mortality and air pollution. As a first step, we included indicators for days of the week to take into account the change in traffic volume between workdays and weekends. We regressed the natural logarithm of the daily death counts on a day sequence to adjust for time trends using either natural or penalized splines. Furthermore, visual inspection of the mortality time series showed that the death counts were significantly higher over the two periods July 28 to August 3, 2003 (sum03), and December 1 to December 31, 2003 (win03). We created a three-level factor variable to indicate the two periods of high mortality and the remaining period. We controlled for the time effects by including in the base model this factor variable and smoothed the terms for the overall periods as well as the three specific periods of high mortality. The three local smoothing terms were accomplished in the s() function with a by= option, where the "by" variable is the sum03 indicator, win03 indicator, or other indicator.

Second, we controlled for potential confounding of relevant weather variables. Daily mortality may depend on weather, possibly in a nonlinear fashion, especially under the condition of high temperatures. We controlled for the weather variables using both (1) indicator variables for extremely hot days, cold days, and humid days and (2) natural splines for the same-day (lag 0 day) temperature and RH. The extremely hot and cold days were defined as those days whose daily average temperatures were above and below the 95th and 5th percentiles, respectively, of the four years of data (Dockery et al. 1992). Similarly, the extremely humid days were defined as those days with an average daily RH above the 95th percentile of the four years of data. The purpose of these two steps was to obtain conservative estimates of the subsequent pollution–mortality associations. Finally, we regressed the effects of the air pollution variables on daily mortality.

In summary, the important covariates in the models are main pollutant effect; days of the week; indicators for extremely cold, hot, and humid days; smooth terms for overall time trend; the two periods of July 28 to August 3, 2003, and December 1 to December 31, 2003; and, last, smooth terms for RH and temperature. Therefore, the generalized additive Poisson model for mortality and a pollutant on any particular day can be expressed as

$$\text{Log E}(y_t) = \alpha + \beta x_{t-l} + \gamma z_t + (1 + \text{I}_{\text{sum03}} + \text{I}_{\text{win03}} + \text{I}_{\text{others}}) \times s(\text{day}_t) + s(\text{humid}_t) + s(\text{temp}_t) \quad (1)$$

Table A.1. Definitions of Variable Names in Core Model Code

Variable Name	Definition
CAUSE	Cause-specific mortality; for example, all natural, cardiovascular, etc.
POLL	PM_{10}, NO_2, SO_2, or O_3
dayseq	Daily time trend
temp	Temperature in Celsius, 1 decimal place
rh	Relative humidity (%)
day_wk	Dummy variables for days of the week; 1 = Monday 2 = Tuesday . . . 6 = Saturday; Sunday = reference
factor_by	Indicator variable for 2 periods July 28, 2003–August 3, 2003 December 1, 2003–December 31, 2003 Period prior to July 28, 2003, between August 3, 2003–December 1, 2003, and after December 31, 2003 = reference
extreme_cold	Indicator variable for extremely cold days (< 5th percentile)
extreme_hot	Indicator variable for extremely hot days (> 95th percentile)
extreme_humid	Indicator variable for extremely humid days (> 95th percentile)
smooth_sum03	Indicator variable for local smoothing over the period July 28, 2003–August 3, 2003
smooth_win03	Indicator variable for local smoothing over the period December 1, 2003–December 31, 2003
smooth_other	Indicator variable for local smoothing over the 4-year period, excluding July 28–August 3, 2003 and December 1–December 31, 2003

Table A.2. Estimates of the Overdispersion Parameter in the Main Models[a]

Cause of Death	PM_{10}	NO_2	SO_2	O_3
All natural	1.335342	1.321038	1.333459	1.384361
Cardiovascular	1.277962	1.277731	1.281287	1.289398
Stroke	1.108433	1.107108	1.113542	1.101003
Cardiac	1.107983	1.108063	1.104645	1.115232
Respiratory	1.360614	1.359240	1.353049	1.360642
Cardiopulmonary	1.337036	1.331831	1.339088	1.365427
Non-cardiopulmonary	1.023273	1.017287	1.022260	1.034477

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothing functions for time, daily mean temperature, and daily mean RH; and local smoothing over 2 peaks of mortality and the remaining period.

where t = 1, 2, . . ., 365 × 4 + 1 indicating the day sequence of the 4-year study period; y_t = the death count on day t; x_{t-l} = the lag l pollutant concentration for day t; l = 0, 1, . . ., 4, 0–1, 0–3; z_t = the vector of controlling variables (e.g., the factor variable for the three periods, and indicator variables for hot days, cold days, and humid days) on day t; I_{sum03}, I_{win03}, and I_{others} = the summer and winter periods in 2003 with high mortality counts and the remaining period; $s(day_t)$, $s(humid_t)$, and $s(temp_t)$ = either natural or penalized splines of the temporal, average RH, and average temperature effects on day t, respectively.

Using this model, we can then estimate, parametrically, the relative change in the logarithmic number of daily deaths per unit increase in the pollutant. The effect estimates are expressed as a percentage change in the mean number of daily deaths per 10-μg/m^3 increase in 24-hour mean concentrations of a pollutant (or in 8-hour mean concentrations for O_3). The associated upper and lower 95% confidence limits are obtained under the assumption that the estimated β is distributed normally. This expression of the research results allows comparison of the magnitude of the estimated effects from this study with those from other published studies.

MODEL SELECTION

There were two steps in building and fitting the model: development of the best base model (without a pollutant) and development of the best main model (with a pollutant).

Development of the Best Base Model

We used sequential methods, a penalized spline method, and a natural spline method to select the best base model for each cause-specific mortality category. The degrees of freedom of the important covariates were determined on the basis of epidemiologic knowledge of the time scale for the major potential confounders, a review of the literature, comments from the HEI International Science Oversight Committee members, and discussion among the investigators from the Air Pollution and Health: A European and North American Approach (APHENA) project and the Public Health and Air Pollution in Asia (PAPA) project. The details of the model construction are described as follows:

Sequential Method

- We fixed the degrees of freedom for the local smoothing functions as 2 df for sum03 and 3 df for win03 based on the length of each time period.
- We started with a reduced model (including only the day of week, extreme weather indicators, time trend, and local smoothing terms). We tried 3 to 8 df for the overall time trend variable and then chose the degrees of freedom that had the smallest sum of the absolute PACF values over a 30-day lag period: $\Sigma_{lag=1}^{30} | \rho_{lag} |$.
- Next, we added temperature to this model using 2 to 4 df. Again, we chose the degrees of freedom that had $\min(\Sigma_{lag=1}^{30} | \rho_{lag} |)$.
- We repeated the same exact process for RH, after including temperature, time trend, day of week, and extreme weather indicators.

Penalized Spline Method We ran the penalized spline model to select the optimal degrees of freedom for the overall time trend, local time intervals, temperature, and RH. We observed that the local smoothing degrees of freedom remain as close to 2 or 3 as they were in the sequential method.

We initialized the degrees of freedom at 8 df for time, 3 df for sum03, 3 df for win03, and 3 df for both temperature and RH — all per year. We tested a few of the disease categories to see if increasing the initial degrees of freedom would change the resulting best base model and found that the higher initial degrees of freedom used with this method resulted in a higher $\Sigma_{lag=1}^{30} | \rho_{lag} |$.

Natural Spline Method We also ran two models (F1 and F2) that used the natural spline method and fixed degrees of freedom for the five smoothing functions, which were labeled (6,2,3,3,3) and (8,2,3,4,4). The five values in parentheses represent the effective degrees of freedom per year for the following: the overall time trend per year; the July 28, 2003, to August 8, 2003, local time smoother (sum03); the December 1, 2003, to December 31, 2003, local time smoother (win03); the temperature smoother for the entire study period; and the RH smoother for the entire study period. Again, these degrees of freedom were chosen based on epidemiologic knowledge, review of the literature, taking into account comments from the HEI International Science Oversight Committee members, and discussion among the investigators from APHENA and PAPA. To select the best base model for each disease category, we always ran the (6,2,3,3,3) and (8,2,3,4,4) models, in addition to the two final models resulting from the use of the sequential method and the penalized spline method. The best base model was determined as the model that has $|\rho| < 0.10$ (where $|\rho|$ represents a PACF residual) for all 30-day lags, and $\min(\Sigma_{lag=1}^{30} | \rho_{lag} |)$ with an expectation of minimizing the effect of unmeasured time-varying confounders on the relations, as expressed in the autocorrelations in the residuals of the outcomes. The former criterion of $|\rho| < 0.10$ took precedence over the latter criterion of $\min(\Sigma_{lag=1}^{30} | \rho_{lag} |)$. To complete the sensitivity analysis, we also tried an alternative order to the sequential method: all deaths due to natural causes, smoothing for temperature, RH, and then time. The new results matched that of the penalized spline method, and therefore, the original sequential result is still more suitable since it has $\min(\Sigma_{lag=1}^{30} | \rho_{lag} |)$. A summary of the best base models are listed in Table 3 in the main text. The residual plots of daily mortality against time after fitting the best base models are shown in Figure 3 in the main text, the PACF residuals plots are shown in Figures B1 through B4 in Appendix B, and plots of observed and predicted deaths are shown in Figures 4A through 4D in the main text.

MAIN MODEL AND LAG ANALYSES

We chose the lag 0–1 day models as the best main models for all pollutants and mortality. However, we also investigated the main effect of the pollutants for various lag terms (lag 0 through lag 4 days individually and the averages of lag 0–3 days).

EXPOSURE–RESPONSE CURVES

Exploring exposure–response relations between daily mortality and daily mean pollutant concentrations is one of the key aims of this study. Several approaches were

taken to investigate the validity of the linearity assumption of PM_{10} expressed in equation (1). First, we plotted the exposure–response curves for the pollutant concentrations and the logarithm of the mortality counts from the fitted GAMs. Specifically, based on the main models, we replaced the linear term of the pollutant concentrations with a smoothing function with 3 df using natural splines. Both the likelihood ratio test with 2 df, which compares the original main model with the smoothed model, and the visual inspection approach were used to assess whether the smoothed exposure–response curve resembled a straight line. Second, in equation (1), we added a quadratic term and tested its statistical significance. Last, we performed piecewise regression analyses by including different slopes of pollutant concentrations taken before and after a cutoff point. The cutoff points for PM_{10}, SO_2, and O_3 were tested from zero to 150 $\mu g/m^3$ for every 25-$\mu g/m^3$ increment, and the cutoff points for NO_2 were tested from zero to 100 $\mu g/m^3$ for every 25-$\mu g/m^3$ increment. We chose the model in which the cutoff point minimized the generalized cross-validation (GCV) value as the best piecewise regression model.

EXTREME WEATHER EFFECTS

Temperature variability has been shown to be an important determinant of short-term ambient air pollution and mortality (Braga et al. 2002). We tested the hypothesis that extreme weather (i.e., both extremely hot and extremely cold temperature) modifies the associations between pollution concentration and mortality. To estimate the pollutant effects on mortality under each of the extremely cold, hot, and normal weather conditions, we first created three corresponding temperature indicators (extreme_cold, extreme_hot, and normal_temp). Next, we included in the models the three pollutant and weather interaction terms without the pollutant main effect (i.e., base model + pollutant × extreme_cold + pollutant × extreme_hot + pollutant × normal_temp). The coefficients of the interaction terms then provided pollutant effect estimates specific to the three weather conditions. To test whether the pollutant effects differ under extreme weather, the models included only the two extreme weather and pollutant interaction terms in addition to the pollutant main effect (i.e., base model + pollutant × extreme_cold + pollutant × extreme_hot + pollutant). The coefficients then provide the differences of the pollutant effects under extreme weather when compared with normal weather conditions.

SENSITIVITY ANALYSES

We needed to determine whether the results were stable and substantially impacted by decisions made during the model construction. Therefore, we performed a wide range of sensitivity analyses to be certain that valid results were obtained. The approaches taken were as follows:

- The best models were used with increasing degrees of freedom up to 12 per year.
- An alternative order was used with the sequential method. The order was changed to smoothing for temperature, RH, and then time.
- Different splines and degrees of freedom were employed. To investigate the impact of different selections for degrees of freedom and different spline methods, we compared the estimated effect of PM_{10} from the best main model with those from the aforementioned (6,2,3,3,3) and (8,2,3,4,4) models as well as with the penalized spline model.
- The influenza season indicator was defined on a weekly basis. A week having total respiratory mortality ≥ the 90th percentile for the respective year was considered an influenza season. We added the influenza season indicator to the main model.
- We included an indicator variable in the model to express the ICD-9-coded mortality data before January 1, 2003, compared with the ICD-10-coded mortality data after December 31, 2002, in order to examine the impact of the switch in ICD coding from ICD-9 to ICD-10.
- We redefined extreme temperature and RH indicators using the 10th percentile of the four years of data (as well as the 3rd, 7th, and 15th percentiles). In addition to lag 0 temperature and RH variables, we added (1) a temperature variable that reflected the daily change (maximum high − minimum low), (2) the lag 1–2 day means of temperature and RH variables, or (3) variables for both lag 1–2 day means of temperature and lag 3–7 day means of RH.
- We included two-pollutant models using the main pollutant plus each of the other three pollutants. For example, when we estimated the PM_{10} main effect, we ran PM_{10} along with SO_2, PM_{10} along with NO_2, and PM_{10} along with O_3.

SUBGROUP ANALYSES

To assess whether putatively susceptible subgroups (e.g., those age ≥ 65 years) have a higher sensitivity to the effects of air pollution, we utilized individual-level information and performed stratified analyses for age and sex. For analyses stratified by age, we used only four levels of analyses (< 65 vs. ≥ 65, and < 45 vs. ≥ 45) because death counts by cause-specific mortality were limited in certain age groups.

ADDITIONAL ANALYSIS OF ICD CODE SWITCH

Since the coding for cause of death in this four-year study (July 1, 2000, to June 30, 2004) changed from ICD-9 to ICD-10 on January 1, 2003, we assessed the potential uncertainty of effect estimates due to the change in coding. To do this, we required each district's center for disease control to recode the 2002 mortality data with ICD-10 coding. Thus, we have both ICD-9- and ICD-10-coded mortality data for the year 2002. We identified any potential difference in pollution mortality estimates due to the shift of ICD coding by examining the concordance rates and kappa statistics between the ICD-9- and ICD-10-coded data as well as by comparing the estimated effect magnitudes obtained from using the two types of ICD-coded mortality data. See Appendix G for a full description of our analysis of the uncertainty of effect estimates due to the change in ICD code.

APPENDIX B. PACF Residuals Plots for Cause-Specific Mortality Using Best Main Model with Lag 0–1 Day Mean

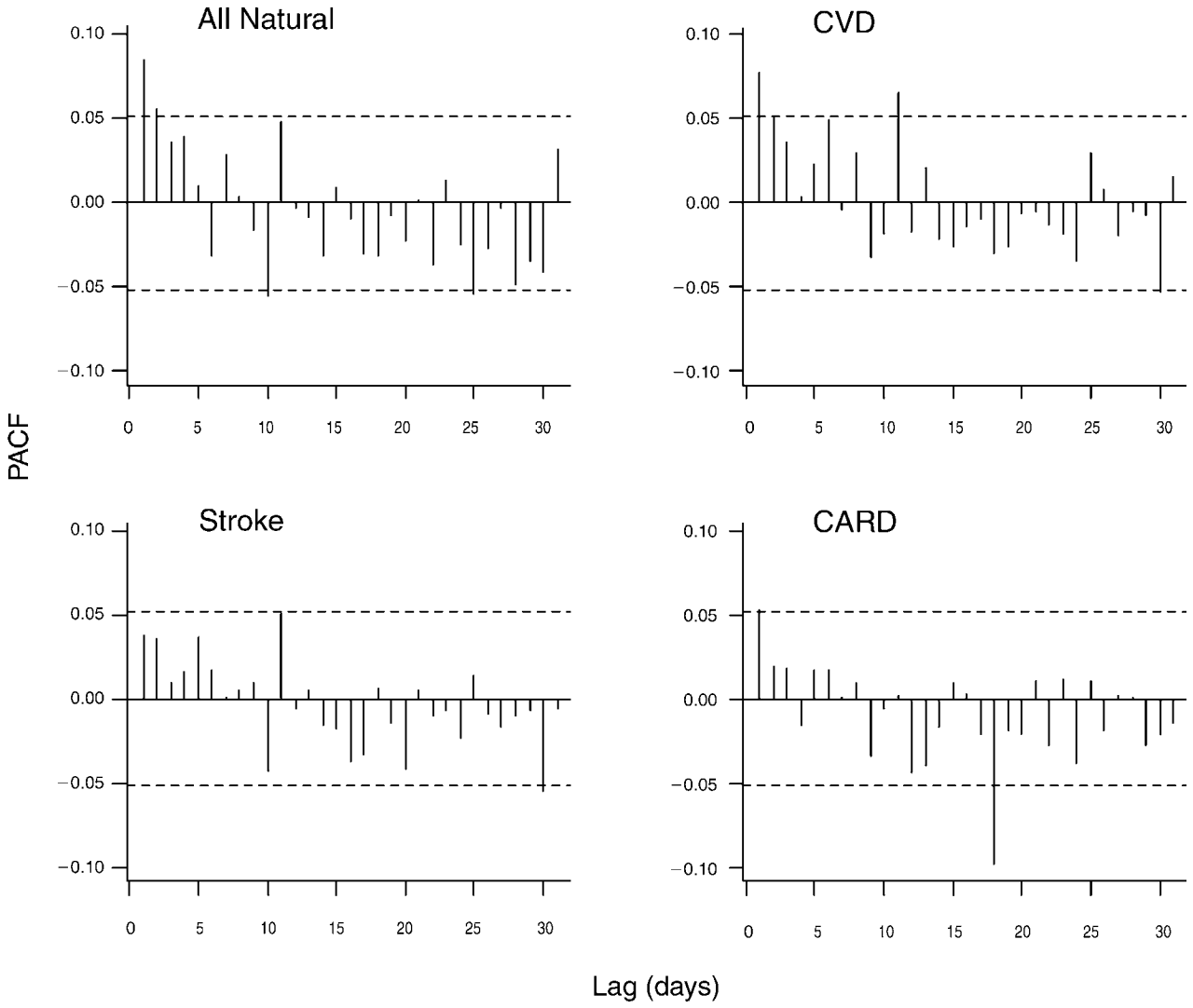

Figure B.1. PACF residuals plots for mortality by cause of death for PM_{10}, using the best main model with lag 0–1 day mean.

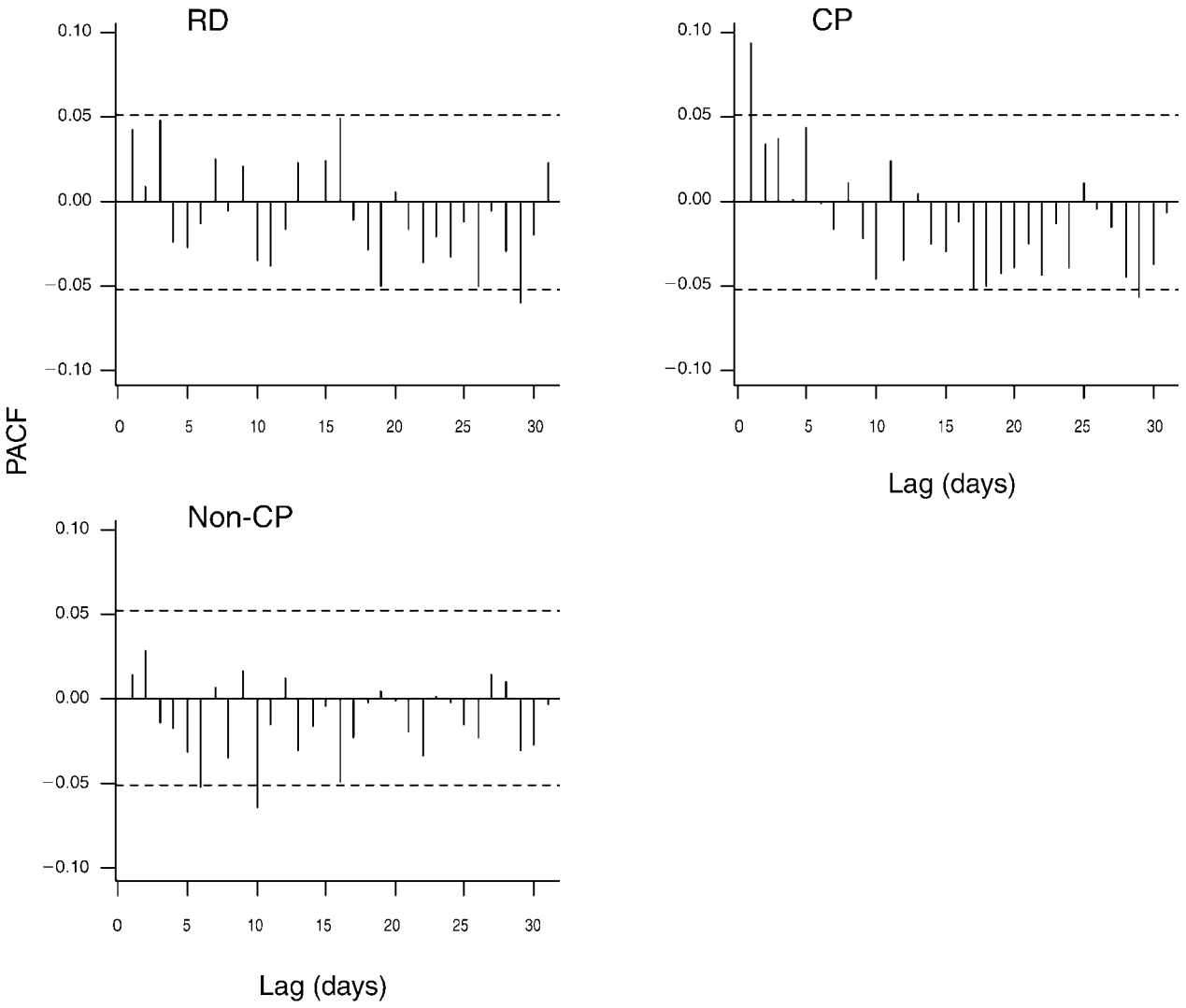

Figure B.1 (*Continued*).

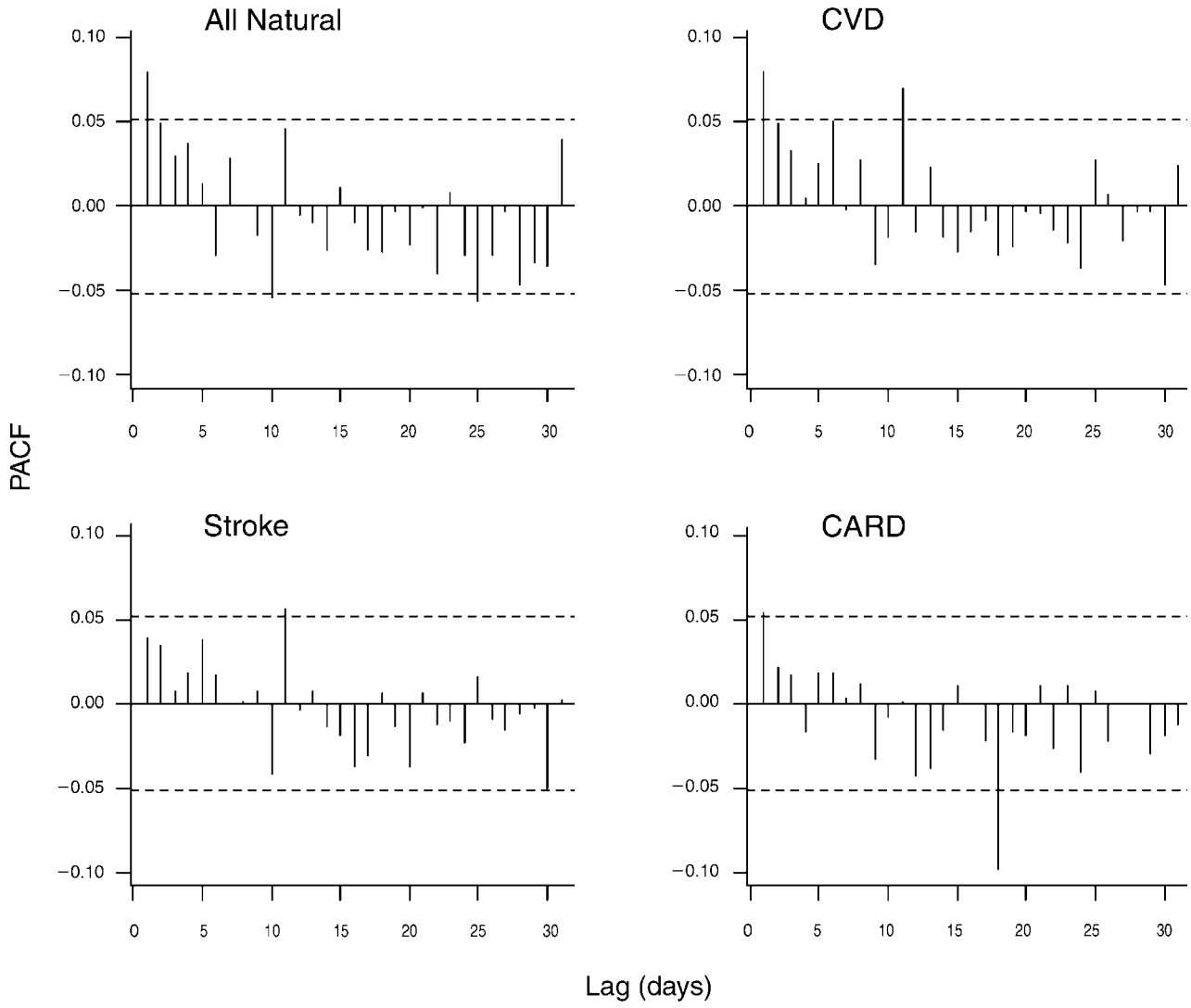

Figure B.2. PACF residuals plots for mortality by cause of death for NO_2, using the best main model with lag 0–1 day mean.

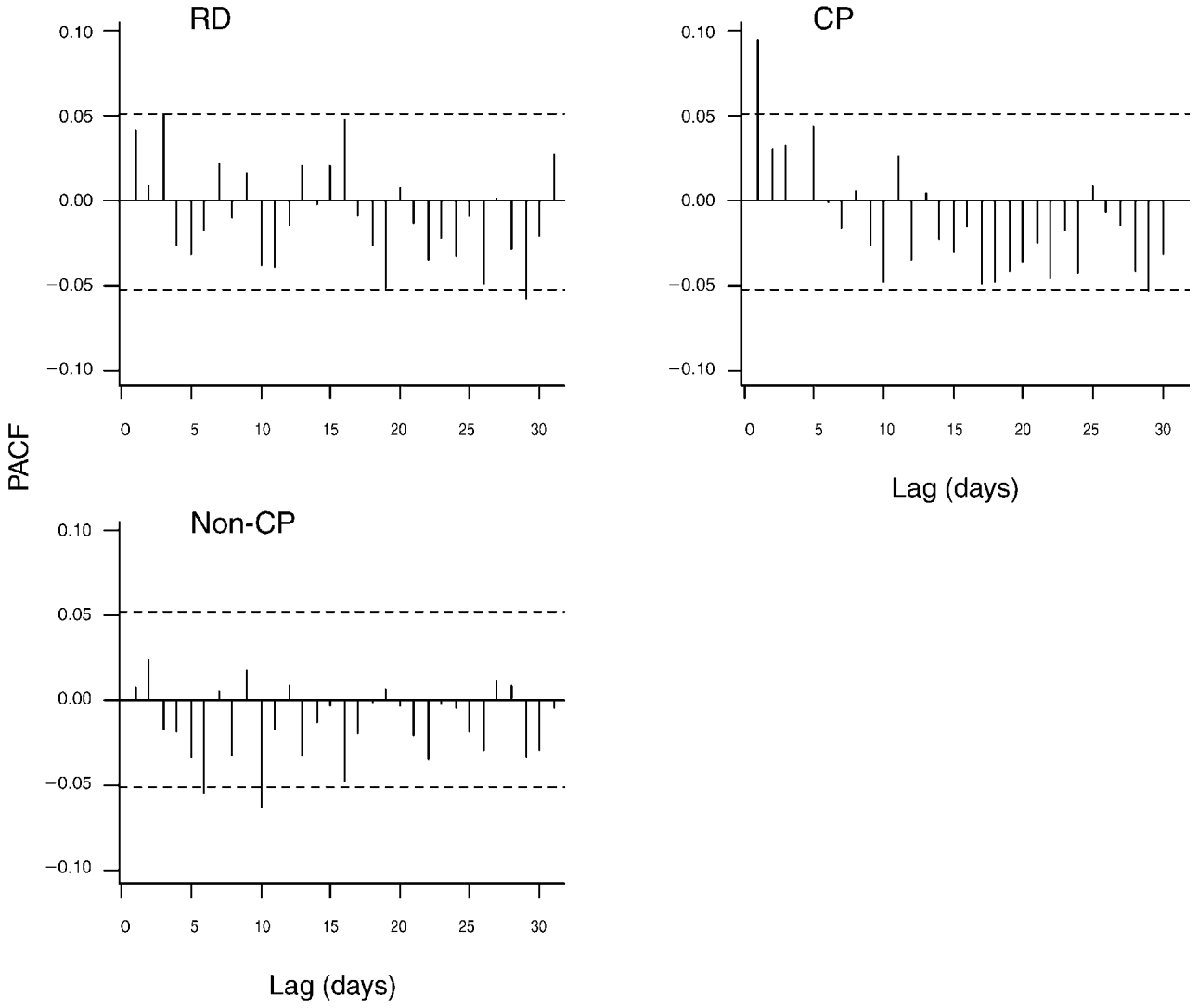

Figure B.2 (*Continued*).

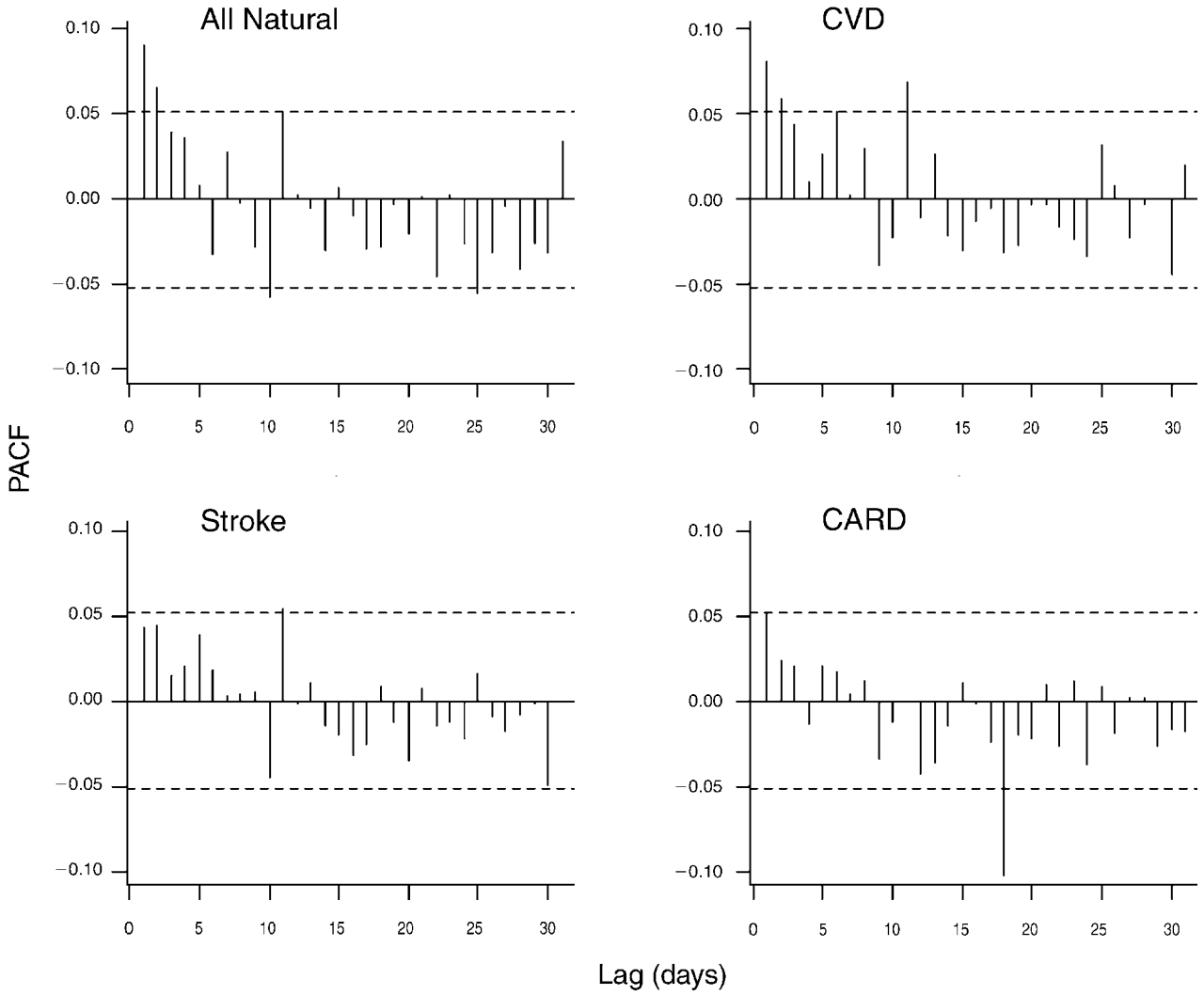

Figure B.3. PACF residuals plots for mortality by cause of death for SO_2, using the best main model with lag 0–1 day mean.

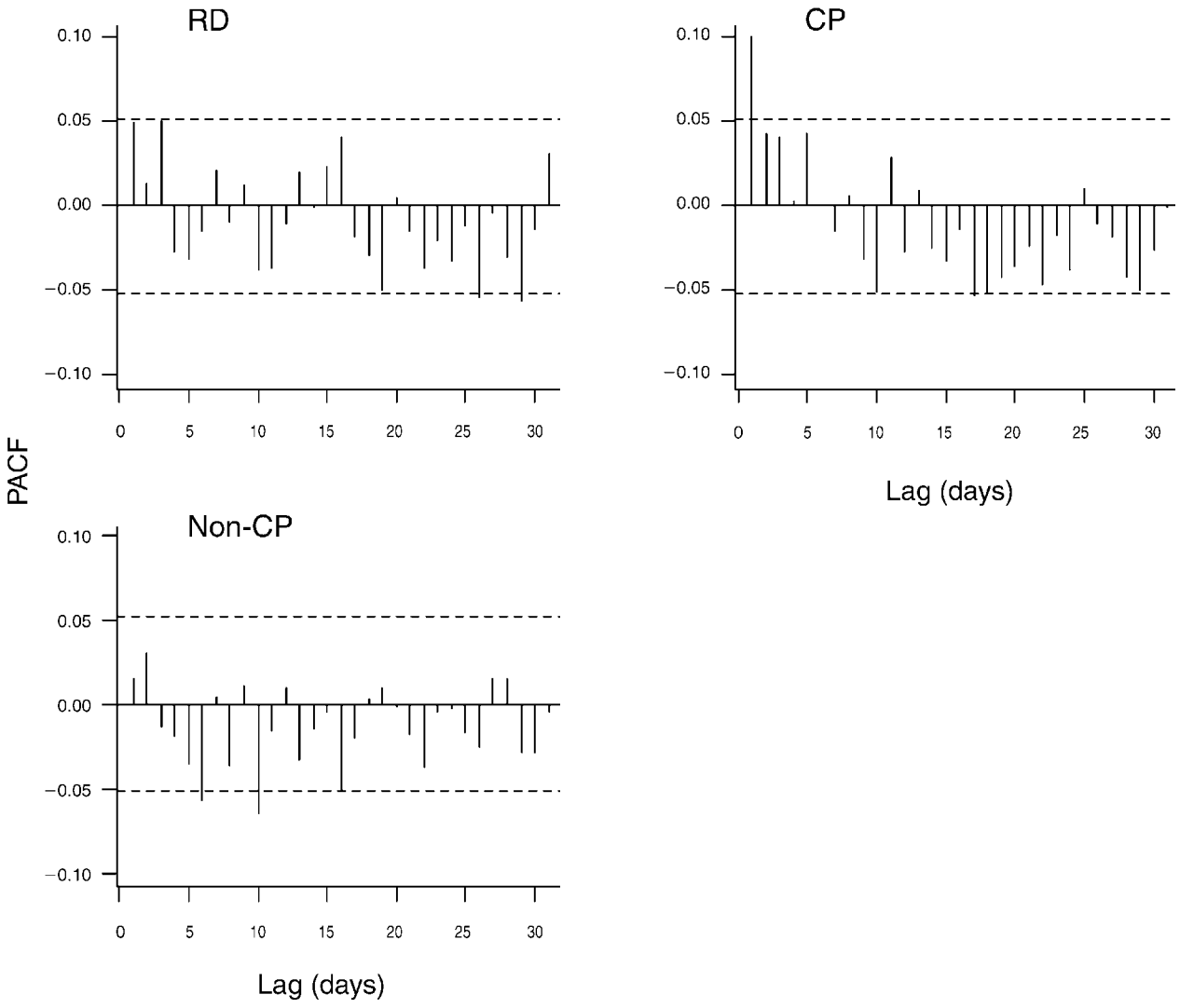

Figure B.3 (*Continued*).

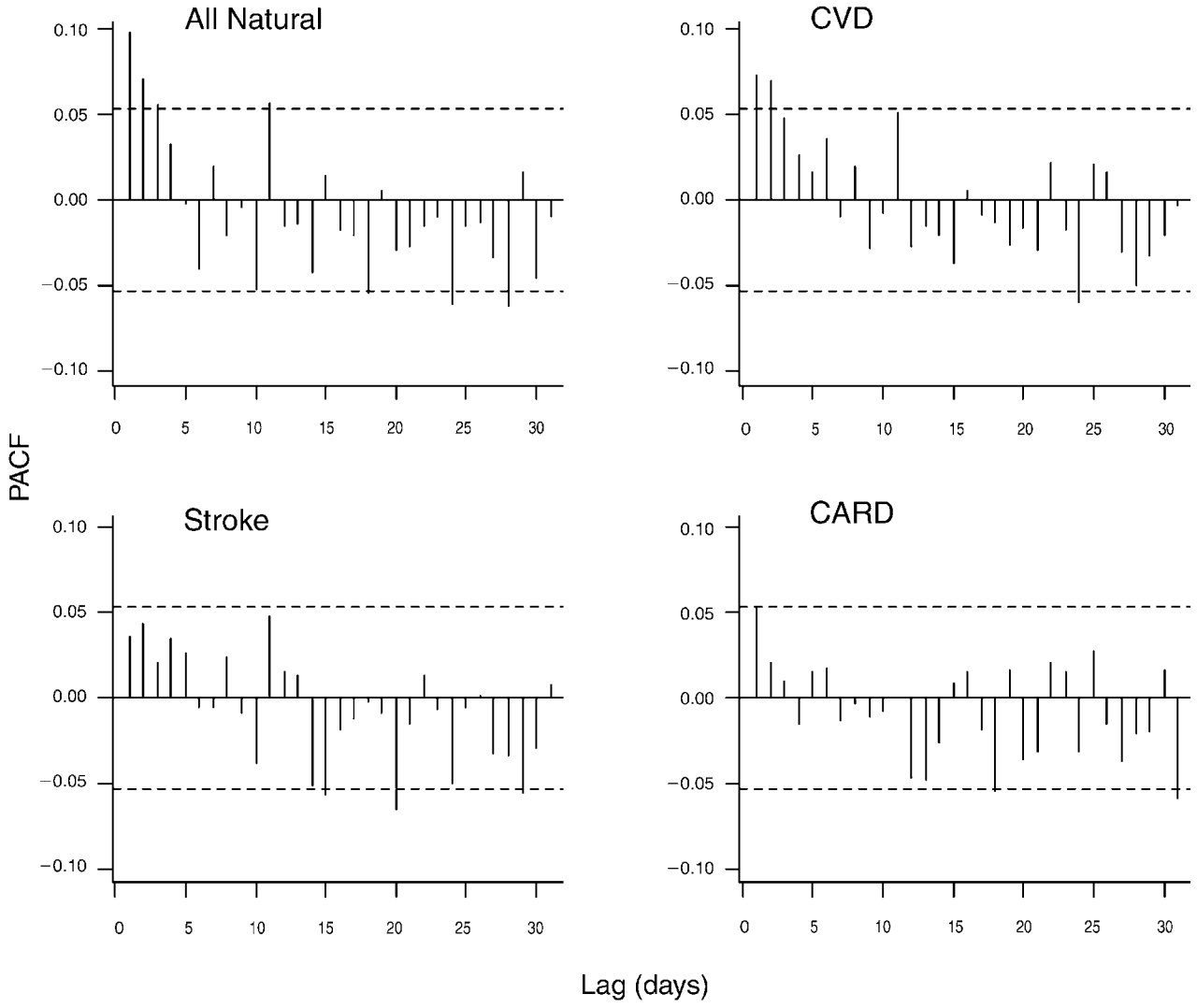

Figure B.4. PACF residuals plots for mortality by cause of death for O_3, using the best main model with lag 0–1 day mean.

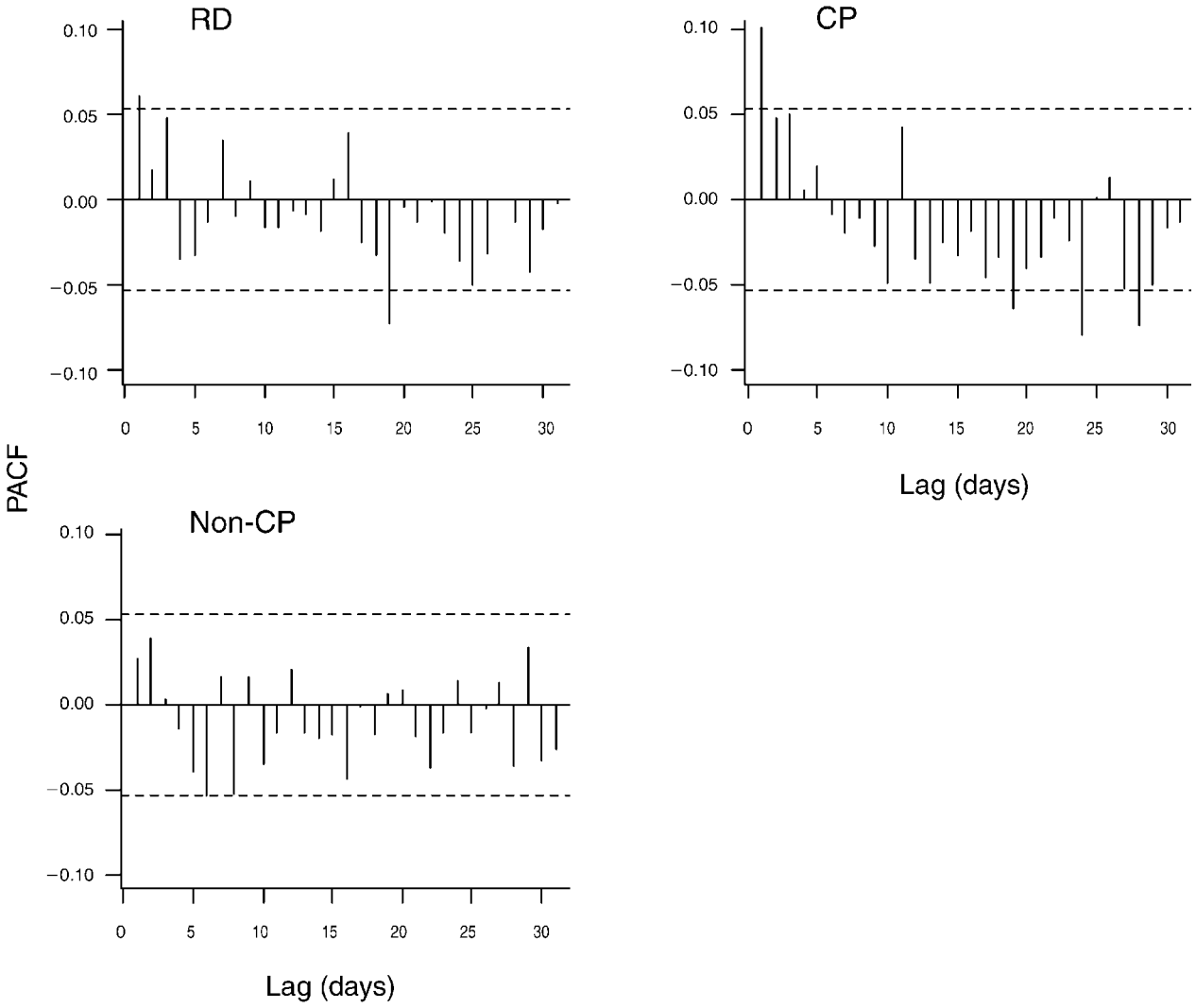

Figure B.4 (*Continued*)

APPENDIX C. Description of Pollutants, Weather, and Mortality Variables

Table C.1. Percentage of Valid Daily Measures of Pollutants from Wuhan Monitoring Stations[a]

Pollutant / Year(s)	Station 1	Station 2	Station 3	Station 4	Station 5	Stations 6/7
PM_{10}						
2001	95.9	96.2	94.2	96.7	95.3	NA
2002	95.6	97.3	96.4	97.5	95.1	NA
2003	97.0	96.7	96.4	94.2	94.8	NA
2004	96.7	93.2	95.6	96.2	92.9	NA
2001–2004	96.3	95.8	95.7	96.2	94.5	NA
O_3[b]						
2001	NA	NA	NA	NA	96.4	97.8
2002	NA	NA	NA	NA	98.1	93.4
2003	NA	NA	NA	NA	97.3	84.1
2004	NA	NA	NA	NA	87.7	73.2
2001–2004	NA	NA	NA	NA	94.9	87.1
NO_2						
2001	95.1	94.2	95.9	95.1	96.7	NA
2002	95.9	90.7	96.7	97.5	97.3	NA
2003	97.0	97.5	99.2	95.6	96.4	NA
2004	94.0	92.3	96.2	95.1	94.3	NA
2001–2004	95.5	93.7	97.0	95.8	96.2	NA
SO_2						
2001	97.5	96.4	95.6	97.8	95.1	NA
2002	97.3	94.0	95.6	97.0	95.6	NA
2003	98.4	97.8	98.4	95.9	96.2	NA
2004	96.7	95.1	95.6	96.4	94.5	NA
2001–2004	97.5	95.8	96.3	96.8	95.3	NA

[a] Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

[b] Only station 5 (Donghu) provided enough valid measurements of O_3; daily 8-hour concentrations (10:00–18:00) were used.

Table C.2. Distribution of Calculated Daily Concentration of Pollutants for the Whole City of Wuhan Using the Centering Approach[a,b]

Pollutant ($\mu g/m^3$) / Year(s)	Number of Valid Observations (n)	Mean	SD	Minimum	Maximum	Percentile		
						25th	50th	75th
PM_{10}								
2001	362	149.8	68.7	43.9	476.3	98.5	133.4	188.1
2002	365	140.4	62.5	40.5	421.9	96.9	125.6	167.5
2003	365	141.9	63.8	33.5	406.3	95.0	133.5	173.9
2004	366	135.1	59.1	17.8	329.2	90.5	126.5	170.5
2001–2004	1458	141.8	63.8	17.8	476.3	94.9	130.2	174.9
NO_2								
2001	361	48.3	16.4	19.0	114.9	36.4	43.9	57.5
2002	365	51.8	19.4	23.4	127.4	39.0	47.1	61.0
2003	365	52.3	19.0	23.8	124.9	38.2	47.3	62.8
2004	366	54.7	19.5	22.1	127.5	39.7	51.6	68.1
2001–2004	1457	51.8	18.7	19.0	127.5	38.1	47.5	62.0
SO_2								
2001	361	34.1	22.3	7.2	115.2	16.7	27.3	43.8
2002	365	37.5	23.7	6.1	119.5	19.0	31.0	49.8
2003	365	41.6	28.5	3.3	187.8	22.0	33.5	55.8
2004	366	43.4	25.2	5.3	169.6	25.7	40.0	54.8
2001–2004	1457	39.2	25.3	3.3	187.8	21.0	32.6	51.8

[a] No centering analysis was performed for O_3 since only O_3 data from station 5 (Donghu) were analyzed.

[b] Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

Table C.3. Distribution of Calculated Daily Concentration of Pollutants for the Whole City of Wuhan Using the Simple Averaging Approach[a]

Pollutant ($\mu g/m^3$) / Year(s)	Number of Valid Observations (*n*)	Mean	SD	Minimum	Maximum	Percentile		
						25th	50th	75th
PM_{10}								
2001	362	149.8	68.7	44.0	477.8	98.2	133.6	188.2
2002	365	140.4	62.6	40.4	421.8	96.4	126.8	167.6
2003	365	141.8	63.8	33.4	406.2	95.0	133.4	173.8
2004	366	135.2	58.8	24.8	330.8	91.0	128.6	169.4
2001–2004	1458	141.8	63.7	24.8	477.8	94.8	130.2	175.0
O_3[b]								
2001	352	88.7	48.4	2.6	224.7	48.6	86.2	124.5
2002	358	87.4	42.4	6.3	245.0	55.8	81.8	116.2
2003	355	85.6	47.6	1.0	258.5	52.0	79.0	115.5
2004	321	80.7	49.7	1.0	242.5	41.3	79.8	117.4
2001–2004	1386	85.7	47.0	1.0	258.5	51.1	81.8	118.5
NO_2								
2001	361	48.3	16.5	19.2	114.8	36.5	44.0	57.4
2002	365	51.6	19.4	23.6	127.4	38.3	47.0	60.8
2003	365	52.4	19.1	23.8	124.8	38.2	47.0	62.8
2004	366	54.7	19.4	22.0	127.4	40.6	51.5	68.2
2001–2004	1457	51.8	18.8	19.2	127.4	38.0	47.2	62.0
SO_2								
2001	361	34.1	22.3	7.3	117.7	16.5	27.0	43.8
2002	365	37.4	23.6	6.3	119.5	19.3	31.3	50.0
2003	365	41.7	28.6	6.3	187.8	21.8	33.5	55.8
2004	366	43.4	25.1	5.3	169.5	25.8	40.0	55.0
2001–2004	1457	39.2	25.3	5.3	187.8	21.0	32.5	51.8

[a] Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

[b] Only station 5 (Donghu) provided enough valid measurements of O_3; daily 8-hour concentrations (10:00–18:00) were used.

Table C.4. Distribution of Daily Concentration of PM_{10}, NO_2, and SO_2 Measured at Station 1 (Jiangan)[a]

Pollutant ($\mu g/m^3$) / Year(s)	Number of Valid Observations (n)	Mean	SD	Minimum	Maximum	Percentile		
						25th	50th	75th
PM_{10}								
2001	350	144.6	77.9	24.0	495.0	86.0	127.0	193.0
2002	349	133.4	69.5	30.0	419.0	84.0	113.0	166.0
2003	354	146.5	72.1	30.0	482.0	94.0	135.0	186.0
2004	354	132.9	61.3	23.0	318.0	87.0	124.5	171.0
2001–2004	1407	139.4	70.6	23.0	495.0	87.0	125.0	180.0
NO_2								
2001	347	54.8	25.7	7.0	167.0	35.0	48.0	70.0
2002	350	58.8	25.3	18.0	155.0	40.0	52.5	73.0
2003	354	63.4	25.4	25.0	151.0	45.0	58.0	79.0
2004	344	62.4	23.9	18.0	146.0	45.0	56.0	79.0
2001–2004	1395	59.9	25.3	7.0	167.0	41.0	54.0	75.0
SO_2								
2001	356	34.8	27.1	2.0	131.0	14.0	26.0	48.0
2002	355	40.0	30.7	5.0	160.0	16.0	31.0	52.0
2003	359	39.5	31.2	3.0	202.0	16.0	33.0	52.0
2004	354	36.6	25.7	3.0	135.0	17.0	30.0	49.0
2001–2004	1424	37.7	28.8	2.0	202.0	16.0	30.0	51.0

[a] O_3 was not monitored at this station. Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

Table C.5. Distribution of Daily Concentration of PM_{10}, NO_2, and SO_2 Measured at Station 2 (Hanyang)[a]

Pollutant ($\mu g/m^3$) / Year(s)	Number of Valid Observations (n)	Mean	SD	Minimum	Maximum	Percentile		
						25th	50th	75th
PM_{10}								
2001	351	147.0	67.8	32.0	460.0	94.0	131.0	187.0
2002	355	137.4	68.9	27.0	465.0	89.0	120.0	174.0
2003	353	148.8	73.1	28.0	495.0	95.0	141.0	187.0
2004	341	151.1	68.0	24.0	408.0	103.0	143.0	189.0
2001–2004	1400	146.0	69.6	24.0	495.0	94.0	133.0	185.0
NO_2								
2001	344	63.5	25.0	7.0	160.0	46.0	57.0	77.0
2002	331	65.6	27.4	23.0	183.0	45.0	61.0	77.0
2003	356	59.8	24.0	21.0	143.0	42.5	54.0	74.5
2004	338	65.5	26.7	22.0	171.0	46.0	61.5	83.0
2001–2004	1369	63.6	25.9	7.0	183.0	45.0	58.0	78.0
SO_2								
2001	352	35.7	28.6	2.0	151.0	13.5	27.0	50.0
2002	343	46.9	30.9	6.0	187.0	24.0	39.0	63.0
2003	357	50.7	39.1	5.0	266.0	23.0	39.0	67.0
2004	348	48.9	31.8	6.0	199.0	26.0	42.0	65.0
2001–2004	1400	45.6	33.4	2.0	266.0	21.0	37.0	62.0

[a] O_3 was not monitored at this station. Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

Table C.6. Distribution of Daily Concentration of PM_{10}, NO_2, and SO_2 Measured at Station 3 (Nanzhan)[a]

Pollutant ($\mu g/m^3$) / Year(s)	Number of Valid Observations (n)	Mean	SD	Minimum	Maximum	Percentile		
						25th	50th	75th
PM_{10}								
2001	344	162.5	75.3	43.0	493.0	106.5	148.5	201.0
2002	352	147.3	75.4	36.0	490.0	96.5	126.0	180.0
2003	352	145.0	67.9	33.0	433.0	96.0	135.0	178.0
2004	350	140.9	64.2	26.0	355.0	93.0	133.0	181.0
2001–2004	1398	148.9	71.2	26.0	493.0	98.0	135.0	186.0
NO_2								
2001	350	50.6	14.7	10.0	102.0	41.0	49.0	59.0
2002	353	56.2	22.6	15.0	159.0	42.0	52.0	66.0
2003	362	59.9	24.3	20.0	164.0	43.0	54.0	74.0
2004	352	60.5	22.3	21.0	152.0	44.0	58.0	73.0
2001–2004	1417	56.8	21.7	10.0	164.0	42.0	52.0	67.0
SO_2								
2001	349	35.4	22.8	4.0	121.0	18.0	29.0	46.0
2002	349	34.3	22.2	3.0	123.0	18.0	29.0	43.0
2003	359	46.4	30.2	7.0	202.0	26.0	38.0	61.0
2004	350	47.8	30.7	5.0	245.0	24.0	43.0	64.0
2001–2004	1407	41.0	27.5	3.0	245.0	21.0	34.0	54.0

[a] O_3 was not monitored at this station. Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

Table C.7. Distribution of Daily Concentration of PM_{10}, NO_2, and SO_2 Measured at Station 4 (Wugang)[a]

Pollutant ($\mu g/m^3$) / Year(s)	Number of Valid Observations (n)	Mean	SD	Minimum	Maximum	Percentile		
						25th	50th	75th
PM_{10}								
2001	353	166.2	63.6	57.0	471.0	120.0	158.0	203.0
2002	356	174.6	63.9	59.0	482.0	130.0	162.0	208.0
2003	344	157.9	67.8	33.0	398.0	113.0	146.0	188.0
2004	352	147.4	62.9	26.0	388.0	100.0	141.5	178.5
2001–2004	1405	161.6	65.3	26.0	482.0	116.0	153.0	195.0
NO_2								
2001	347	39.2	11.4	11.0	77.0	31.0	39.0	46.0
2002	356	43.2	16.1	8.0	103.0	31.0	41.0	52.0
2003	349	44.0	14.8	8.0	100.0	34.0	42.0	51.0
2004	348	47.2	16.8	11.0	98.0	35.0	45.0	57.0
2001–2004	1400	43.4	15.2	8.0	103.0	33.0	41.0	52.0
SO_2								
2001	357	53.1	46.4	4.0	370.0	23.0	42.0	70.0
2002	354	61.7	62.9	6.0	485.0	23.0	42.5	74.0
2003	350	71.0	71.0	5.0	410.0	27.0	51.0	81.0
2004	353	70.9	76.9	3.0	599.0	27.0	51.0	83.0
2001–2004	1414	64.1	65.6	3.0	599.0	25.0	46.0	76.0

[a] O_3 was not monitored at this station. Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

Table C.8. Distribution of Daily Concentration of PM_{10}, O_3, NO_2, and SO_2 Measured at Station 5 (Donghu)[a,b]

Pollutant ($\mu g/m^3$) / Year(s)	Number of Valid Observations (n)	Mean	SD	Minimum	Maximum	Percentile		
						25th	50th	75th
PM_{10}								
2001	348	129.9	67.2	24.0	485.0	80.0	119.0	164.5
2002	347	108.5	48.3	29.0	321.0	76.0	97.0	127.0
2003	346	110.4	51.4	24.0	331.0	75.0	103.0	138.0
2004	340	106.4	46.6	21.0	266.0	73.0	102.0	135.0
2001–2004	1381	113.9	54.8	21.0	485.0	76.0	104.0	142.0
O_3								
2001	352	88.7	48.4	2.6	224.7	48.6	86.2	124.5
2002	358	87.4	42.4	6.3	245.0	55.8	81.8	116.2
2003	355	85.6	47.6	1.0	258.5	52.0	79.0	115.5
2004	321	80.7	49.7	1.0	242.5	41.3	79.8	117.4
2001–2004	1386	85.7	47.0	1.0	258.5	51.1	81.8	118.5
NO_2								
2001	353	34.2	16.3	4.0	119.0	22.0	31.0	44.0
2002	355	35.2	17.0	10.0	111.0	24.0	31.0	42.0
2003	352	34.4	16.5	8.0	103.0	22.0	31.0	42.0
2004	345	39.4	17.6	4.0	120.0	26.0	36.0	48.0
2001–2004	1405	35.8	17.0	4.0	120.0	24.0	32.0	44.0
SO_2								
2001	347	30.7	17.6	3.0	96.0	17.0	27.0	41.0
2002	349	29.0	21.3	3.0	152.0	13.0	23.0	40.0
2003	351	29.8	19.8	3.0	122.0	15.0	26.0	39.0
2004	346	41.4	25.6	3.0	174.0	22.0	37.0	55.0
2001–2004	1393	32.7	21.9	3.0	174.0	16.0	27.0	45.0

[a] Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

[b] Only station 5 (Donghu) provided enough valid measurements of O_3; daily 8-hour concentrations (10:00–18:00) were used.

Table C.9. Distribution of Daily Concentration of O_3 Measured at Stations 6 and 7 (Jiantan/Kifa)[a,b]

Pollutant ($\mu g/m^3$) / Year(s)	Number of Valid Observations (n)	Mean	SD	Minimum	Maximum	Percentile		
						25th	50th	75th
O_3								
2001	357	60.0	35.5	1.0	154.8	31.3	56.9	84.0
2002	341	72.1	42.6	1.0	196.1	41.4	68.0	97.1
2003	307	70.6	41.2	1.4	216.4	39.1	66.5	95.6
2004	268	90.1	41.2	1.0	210.5	60.3	90.4	116.1
2001–2004	1273	72.2	41.4	1.0	216.4	40.9	69.4	98.6

[a] The O_3 monitoring station was relocated from Kifa to Jiantan on January 12, 2004.

[b] Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

Table C.10. Distribution of Weather Variables by Year[a]

Weather Variable / Year(s)	Number of Valid Observations (n)	Mean	SD	Minimum	Maximum	Percentile		
						25th	50th	75th
Daily mean temperature (°C)								
2001	365	17.7	9.4	−0.4	34.7	8.9	18.1	26.5
2002	365	18.5	9.0	0.6	34.1	11.0	18.0	26.8
2003	365	17.4	9.3	−2.5	34.7	9.3	18.5	25.3
2004	366	18.1	9.1	0.3	35.8	9.7	19.8	25.1
2001–2004	1461	17.9	9.2	−2.5	35.8	9.7	18.5	26.0
Daily mean RH (%)								
2001	365	76.6	12.2	38.0	98.0	68.0	78.0	85.0
2002	365	73.4	12.6	38.0	98.0	64.0	72.0	84.0
2003	365	74.9	11.8	37.0	97.0	66.0	75.0	84.0
2004	366	71.2	12.8	35.0	99.0	62.0	71.0	81.0
2001–2004	1461	74.0	12.5	35.0	99.0	65.0	74.0	84.0

[a] Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

Table C.11. Daily Mortality by Cause of Death and Age Group, July 1, 2000, to June 30, 2004

Cause of Death[a] / Age (Years)	Total Number of Deaths	Number of Days With No Deaths	Mean	Variance	Variance/ Mean	Minimum	Maximum	Percentile 25th	Percentile 50th	Percentile 75th
All natural	89,131	0	61.0	248.9	4.08	25	213	51	59	69
< 45	7,185	11	4.9	5.5	1.12	0	17	3	5	6
≥ 45	81,946	0	56.1	233.0	4.15	23	196	46	54	64
< 65	25,076	0	17.2	22.6	1.32	6	54	14	17	20
≥ 65	64,055	0	43.8	179.8	4.10	18	159	35	41	50
Cardiovascular	40,623	0	27.8	77.9	2.80	8	94	22	27	33
< 45	1,221	631	0.8	0.8	0.98	0	5	0	1	1
≥ 45	39,402	0	27.0	75.1	2.79	8	92	21	26	32
< 65	7,945	15	5.4	6.8	1.24	0	17	4	5	7
≥ 65	32,678	0	22.4	59.7	2.67	6	77	17	21	26
Stroke	25,557	0	17.5	34.8	1.99	4	57	13	17	21
< 45	632	940	0.4	0.4	0.96	0	4	0	0	1
≥ 45	24,925	0	17.1	33.8	1.98	4	57	13	16	20
< 65	5,148	54	3.5	4.2	1.19	0	13	2	3	5
≥ 65	20,409	0	14.0	27.0	1.93	2	52	10	13	17
Cardiac	12,166	2	8.3	13.8	1.66	0	29	6	8	11
< 45	510	1023	0.4	0.3	0.98	0	4	0	0	1
≥ 45	11,656	2	8.0	13.1	1.64	0	29	5	8	10
< 65	2,327	300	1.6	1.7	1.08	0	7	1	1	2
≥ 65	9,839	6	6.7	10.5	1.55	0	25	4	6	8
Respiratory	10,287	9	7.0	33.4	4.75	0	125	4	6	9
< 45	226	1268	0.3	0.3	1.64	0	12	0	0	0
≥ 45	10,061	9	6.9	31.0	4.50	0	113	4	6	9
< 65	1,139	722	0.8	1.8	2.30	0	34	0	1	1
≥ 65	9,148	12	6.3	24.2	3.87	0	91	3	5	8
Cardiopulmonary	50,910	0	34.9	159.1	4.56	11	185	27	32	41
< 45	1,447	556	1.0	1.2	1.16	0	15	0	1	2
≥ 45	49,463	0	33.9	152.2	4.50	11	170	26	32	40
< 65	9,084	6	6.2	9.1	1.46	0	44	4	6	8
≥ 65	41,826	0	28.6	121.4	4.24	9	141	21	26	34
Non-cardiopulmonary	38,221	0	26.2	34.2	1.31	10	53	22	26	30
< 45	5,738	38	3.9	4.3	1.09	0	12	2	4	5
≥ 45	32,483	0	22.2	29.4	1.32	6	47	19	22	26
< 65	15,992	0	11.0	11.2	1.03	1	25	9	11	13
≥ 65	22,229	0	15.2	20.0	1.31	4	37	12	15	18

[a] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table C.12. Characteristics of Deceased Residents of Wuhan at Time of Death[a]

Characteristics	Total Deaths	%
Year of death		
2001	22,561	25.31
2002	21,636	24.27
2003	22,253	24.97
2004	22,681	25.45
2001–2004	89,131	100.00
Sex		
Male	49,457	55.49
Female	39,674	44.51
Age		
0–4	1,322	1.48
5–44	5,863	6.58
45–64	17,891	20.07
≥ 65	64,055	71.87
≥ 45	81,946	91.94
Underlying cause of death[b]		
All natural causes	89,131	100.00
Cardiovascular diseases	40,623	45.58
Cerebrovascular disease or stroke	25,557	28.67
Cardiac or heart disease	12,166	13.65
Respiratory	10,287	11.54
Cardiopulmonary	50,910	57.12
Non-cardiopulmonary	38,221	42.88

[a] Year 2001 = July 1, 2000, to June 30, 2001; Year 2002 = July 1, 2001, to June 30, 2002; Year 2003 = July 1, 2002, to June 30, 2003; and Year 2004 = July 1, 2003, to June 30, 2004.

[b] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table C.13. Beta Coefficients for Two-Pollutant Regressions with Adjustment for Seasonal and Weather Variables, July 1, 2000, to June 30, 2004[a]

Pollutants	Intercept (SE)	Slope (SE)
PM_{10}		
NO_2	4.8527 (0.7407)	0.0112 (0.0004)
SO_2	5.0700 (0.0868)	0.0040 (0.0004)
O_3	4.9243 (0.1648)	0.0009 (0.0003)
NO_2		
PM_{10}	3.4520 (0.5965)	0.0029 (0.0001)
SO_2	3.7720 (0.6224)	0.0071 (0.0003)
O_3	3.6568 (0.1369)	0.0016 (0.0002)
SO_2[b]		
PM_{10}	3.3580 (0.9565)	0.0021 (0.0002)
NO_2	3.3230 (0.8258)	0.0138 (0.0006)
O_3	3.5890 (0.1845)	0.0023 (0.0004)
O_3[c]		
PM_{10}	4.0026 (0.3926)	0.0007 (0.0002)
NO_2	3.8866 (0.3813)	0.0054 (0.0007)
SO_2	3.9659 (0.3832)	0.0039 (0.0006)

[a] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothing functions for time, daily mean temperature, and daily mean RH; and local smoothing over 2 peaks of mortality and the remaining period.

[b] Excluding station 4 (Wugang).

[c] Only station 5 (Donghu) provided valid measurements of O_3; daily 8-hour concentrations (10:00–18:00) were used.

Table C.14. Daily Mortality by Cause of Death and Age Group, July 1, 2000, to June 30, 2004

Cause of Death[a] / Age (Years)	Total Number of Deaths	Number of Days with No Deaths	Mean	Variance	Variance/ Mean	Mini-mum	Maxi-mum	Percentile		
								25th	50th	75th
All natural	89,131	0	61.01	248.93	4.08	25	213	51	59	69
0–4	1,322	623	0.90	1.06	1.17	0	7	0	1	1
5–44	5,863	25	4.01	4.53	1.13	0	17	2	4	5
45–64	17,891	0	12.25	15.66	1.28	2	37	9	12	15
≥ 65	64,055	0	43.84	179.78	4.10	18	159	35	41	50
≥ 45	81,946	0	56.09	233.00	4.15	23	196	46	54	64
Cardiovascular	40,623	0	27.80	77.85	2.80	8	94	22	27	33
0–4	8	1453	0.01	0.01	1.00	0	1	0	0	0
5–44	1,213	635	0.83	0.82	0.99	0	5	0	1	1
45–64	6,724	26	4.60	5.71	1.24	0	15	3	4	6
≥ 65	32,678	0	22.37	59.66	2.67	6	77	17	21	26
≥ 45	39,402	0	26.97	75.14	2.79	8	92	21	26	32
Stroke	25,557	0	17.49	34.81	1.99	4	57	13	17	21
0–4	1	1460	0.00	0.00	1.00	0	1	0	0	0
5–44	631	941	0.43	0.42	0.96	0	4	0	0	1
45–64	4,516	82	3.09	3.75	1.21	0	13	2	3	4
≥ 65	20,409	0	13.97	27.00	1.93	2	52	10	13	17
≥ 45	24,925	0	17.06	33.81	1.98	4	57	13	16	20
Cardiac	12,166	2	8.33	13.80	1.66	0	29	6	8	11
0–4	7	1454	0.00	0.00	1.00	0	1	0	0	0
5–44	503	1029	0.34	0.34	0.98	0	4	0	0	1
45–64	1,817	426	1.24	1.32	1.06	0	7	0	1	2
≥ 65	9,839	6	6.73	10.46	1.55	0	25	4	6	8
≥ 45	11,656	2	7.98	13.07	1.64	0	29	5	8	10
Respiratory	10,287	9	7.04	33.43	4.75	0	125	4	6	9
0–4	27	1438	0.02	0.02	1.28	0	2	0	0	0
5–44	199	1289	0.14	0.23	1.71	0	12	0	0	0
45–64	913	828	0.62	1.14	1.82	0	22	0	0	1
≥ 65	9,148	12	6.26	24.24	3.87	0	91	3	5	8
≥ 45	10,061	9	6.89	30.99	4.50	0	113	4	6	9
Cardiopulmonary	50,910	0	34.85	159.05	4.56	11	185	27	32	41
0–4	35	1431	0.02	0.03	1.26	0	2	0	0	0
5–44	1,412	569	0.97	1.12	1.16	0	15	0	1	1
45–64	7,637	14	5.23	7.15	1.37	0	29	3	5	7
≥ 65	41,826	0	28.63	121.44	4.24	9	141	21	26	34
≥ 45	49,463	0	33.86	152.22	4.50	11	170	26	32	40
Non-cardiopulmonary	38,221	0	26.16	34.15	1.31	10	53	22	26	30
0–4	1,287	640	0.88	1.04	1.18	0	7	0	1	1
5–44	4,451	80	3.05	3.23	1.06	0	10	2	3	4
45–64	10,254	2	7.02	7.18	1.02	0	19	5	7	9
≥ 65	22,229	0	15.21	19.95	1.31	4	37	12	15	18
≥ 45	32,483	0	22.23	29.44	1.32	6	47	19	22	26

[a] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table C.15. Monitor-to-Monitor Pearson Correlation Coefficients for Specific Pollutants[a]

	Station 1	Station 2	Station 3	Station 4	Station 5
PM_{10}					
Station 1	1.00	0.97	0.95	0.83	0.92
Station 2	0.97	1.00	0.96	0.83	0.92
Station 3	0.95	0.96	1.00	0.85	0.94
Station 4	0.83	0.83	0.85	1.00	0.86
Station 5	0.92	0.92	0.94	0.86	1.00
NO_2					
Station 1	1.00	0.83	0.75	0.59	0.75
Station 2	0.83	1.00	0.84	0.65	0.71
Station 3	0.75	0.84	1.00	0.76	0.75
Station 4	0.59	0.65	0.76	1.00	0.69
Station 5	0.75	0.71	0.75	0.69	1.00
SO_2					
Station 1	1.00	0.82	0.69	0.00	0.63
Station 2	0.82	1.00	0.84	0.05	0.69
Station 3	0.69	0.84	1.00	0.16	0.75
Station 4	0.00	0.05	0.16	1.00	0.13
Station 5	0.63	0.69	0.75	0.13	1.00

[a] Only station 5 (Donghu) provided valid measurements of O_3.

Table C.16. Pearson Correlation Coefficients Between Pollutants by Monitor[a]

	PM_{10}	NO_2	SO_2	O_3
Station 1				
PM_{10}	1.00	0.74	0.66	NA
NO_2	—	1.00	0.77	NA
SO_2	—	—	1.00	NA
Station 2				
PM_{10}	1.00	0.70	0.61	NA
NO_2	—	1.00	0.70	NA
SO_2	—	—	1.00	NA
Station 3				
PM_{10}	1.00	0.69	0.49	NA
NO_2	—	1.00	0.67	NA
SO_2	—	—	1.00	NA
Station 4				
PM_{10}	1.00	0.63	0.29	NA
NO_2	—	1.00	0.48	NA
SO_2	—	—	1.00	NA
Station 5				
PM_{10}	1.00	0.60	0.48	0.04
NO_2	—	1.00	0.57	−0.10
SO_2	—	—	1.00	−0.01
O_3	—	—	—	1.00

[a] Only station 5 (Donghu) provided valid measurements of O_3 (NA indicates not available).

Table C.17. Correlations and Trends in Measured Ambient Air Pollutants by Temperature, July 1, 2000, to June 30, 2004[a,b]

Pollutant ($\mu g/m^3$) / Temperature	Number of Monitoring Stations	Range of Mean Values Between Stations	Coefficient of Variation of Daily Mean (%)	Range of Pearson Correlation Coefficients Between Monitoring Stations	Means of Daily Means	
					Mean	Average Annual Change[c]
PM_{10}						
Normal	5	116.9–166.1	44.3	0.83–0.97	145.7	−4.5
Low	5	95.5–126.6	42.2	0.76–0.97	117.3	4.3
High	5	72.7–118.6	28.9	0.50–0.93	96.3	−1.5
O_3						
Normal	1	NA	54.3	NA	87.4	−2.8
Low	1	NA	47.7	NA	51.5	4.6
High	1	NA	45.5	NA	91.9	−3.0
SO_2						
Normal	4	32.8–45.9	64.4	0.64–0.84	39.4	3.3
Low	4	41.3–58.7	53.0	0.61–0.87	50.3	4.0
High	4	17.4–28.1	42.9	0.27–0.78	23.8	2.6
NO_2						
Normal	5	36.3–64.8	35.3	0.57–0.84	52.9	2.1
Low	5	37.6–61.9	34.8	0.69–0.86	51.2	3.3
High	5	22.3–43.2	19.1	0.11–0.66	32.5	1.3

[a] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

[b] NA indicates not available.

[c] Calculated from a linear regression model.

Table C.18. Daily Mortality by Cause of Death and Temperature, July 1, 2000, to June 30, 2004[a]

Cause of Death[b] / Temperature	Total Number of Deaths	Number of Days with No Deaths	Mean	Variance	Variance/ Mean	Minimum	Maximum	Percentile 25th	50th	75th
All natural										
Normal	78,666	0	59.82	216.23	3.61	25	213	50	58	67
Low	5,839	0	79.99	142.96	1.79	57	107	71	80	88
High	4,626	0	63.37	562.10	8.87	40	156	51	56	68
Cardiovascular										
Normal	35,684	0	27.14	65.75	2.42	8	67	21	26	32
Low	2,815	0	38.56	56.78	1.47	26	60	33	37	43
High	2,124	0	29.10	194.73	6.69	11	94	22	26	32
Stroke										
Normal	22,544	0	17.14	31.24	1.82	4	43	13	17	21
Low	1,713	0	23.47	25.97	1.11	14	35	20	23	27
High	1,300	0	17.81	71.27	4.00	6	57	13	16	20
Cardiac										
Normal	10,634	2	8.09	12.09	1.50	0	22	6	8	10
Low	898	0	12.30	16.88	1.37	3	23	9	12	15
High	634	0	8.68	25.11	2.89	2	29	5	8	11
Respiratory										
Normal	8,894	9	6.76	32.14	4.75	0	125	4	6	8
Low	894	0	12.25	15.86	1.29	5	25	9	13	15
High	499	0	6.84	46.50	6.80	1	56	4	5	8
Cardiopulmonary										
Normal	44,578	0	33.90	137.88	4.07	11	185	26	32	39
Low	3,709	0	50.81	87.88	1.73	33	78	44	50	56
High	2,623	0	35.93	345.09	9.60	15	111	27	32	38
Non-cardiopulmonary										
Normal	34,088	0	25.92	31.97	1.23	10	46	22	26	30
Low	2,130	0	29.18	49.37	1.69	13	45	25	28	34
High	2,003	0	27.44	47.83	1.74	15	53	23	26	30

[a] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

[b] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

APPENDIX D. Time-Series Plots of Pollutant Concentrations by Monitor

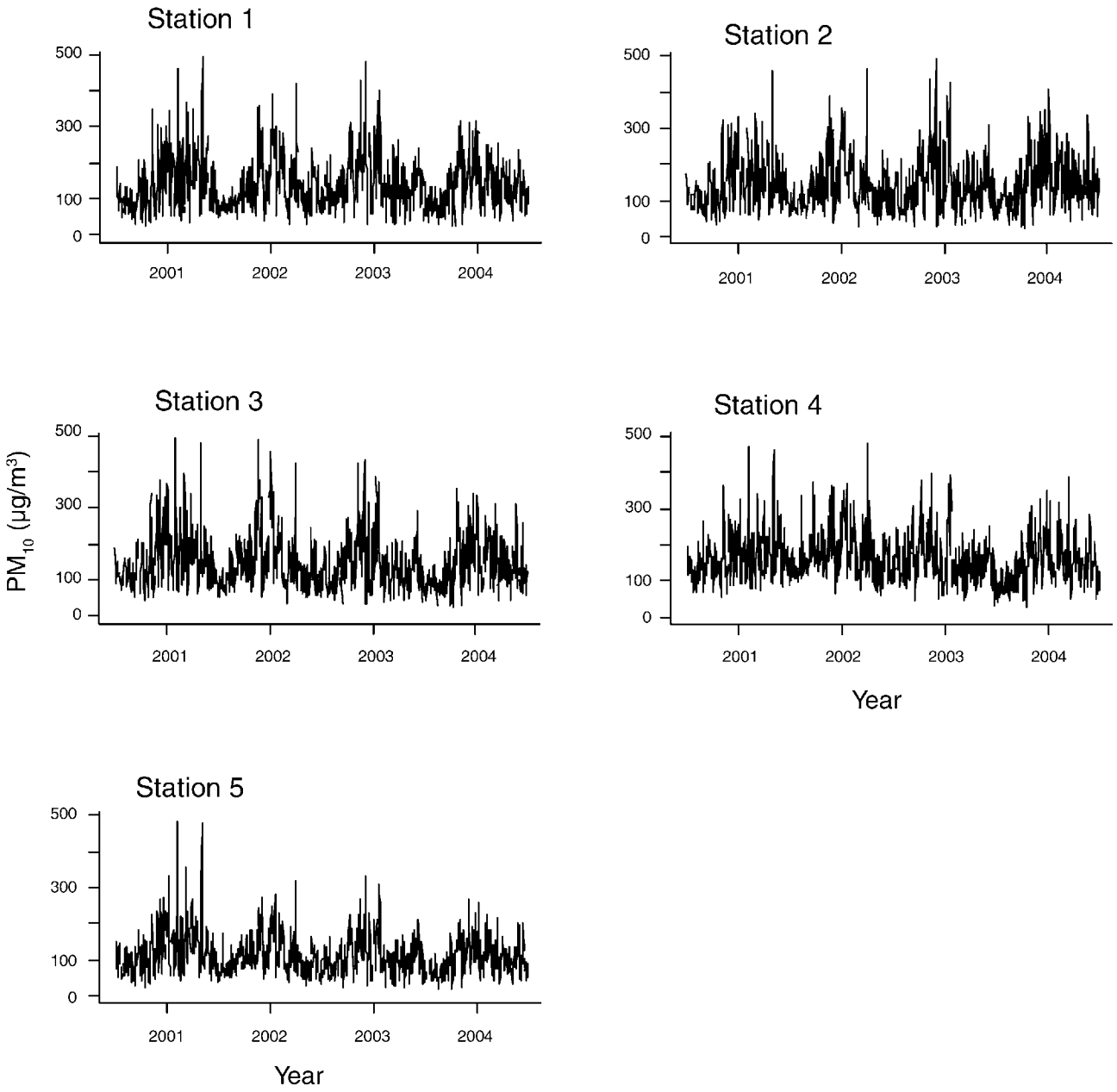

Figure D.1. Time-series plots of PM_{10} concentrations by monitor.

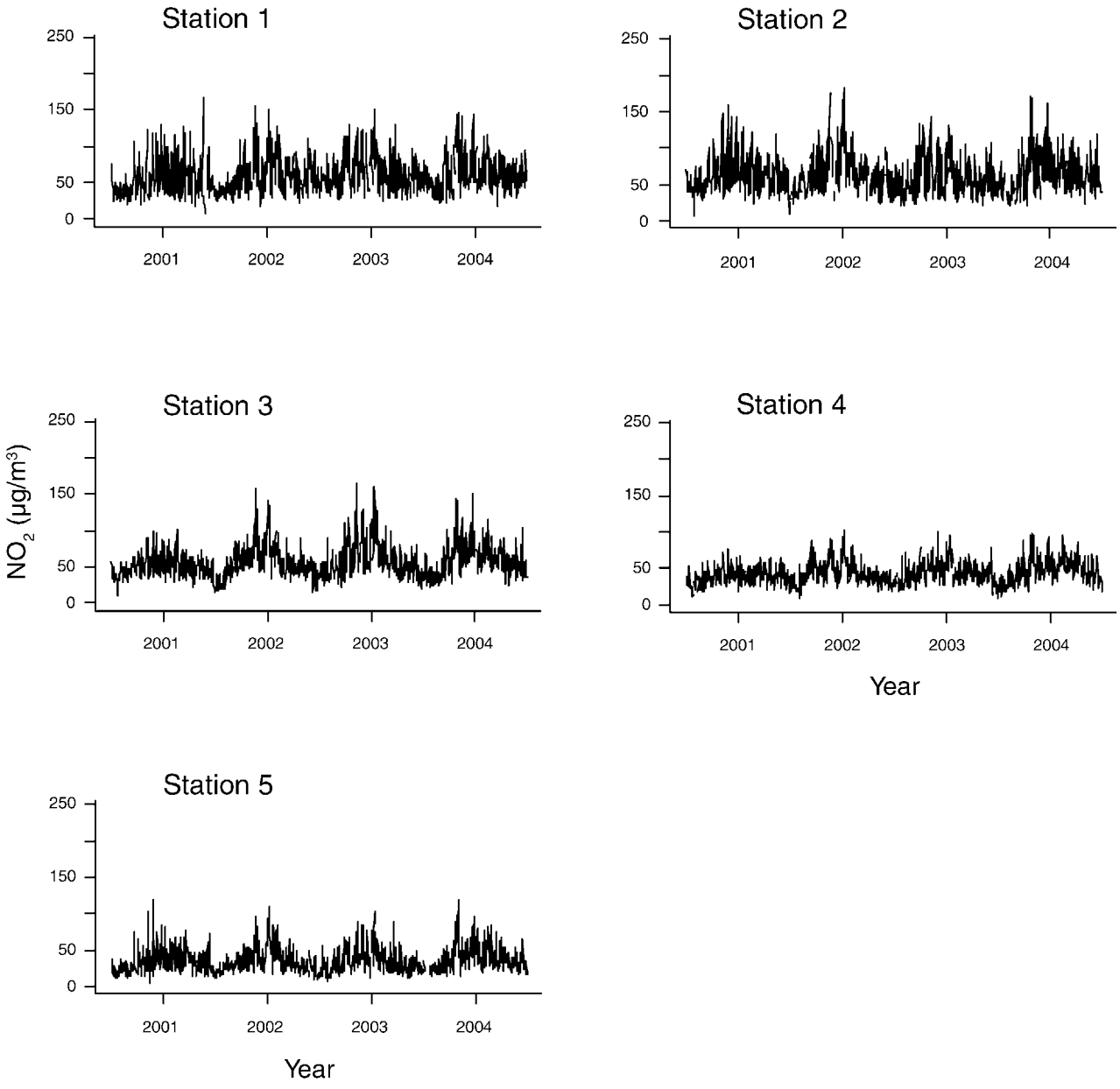

Figure D.2. Time-series plots of NO_2 concentrations by monitor.

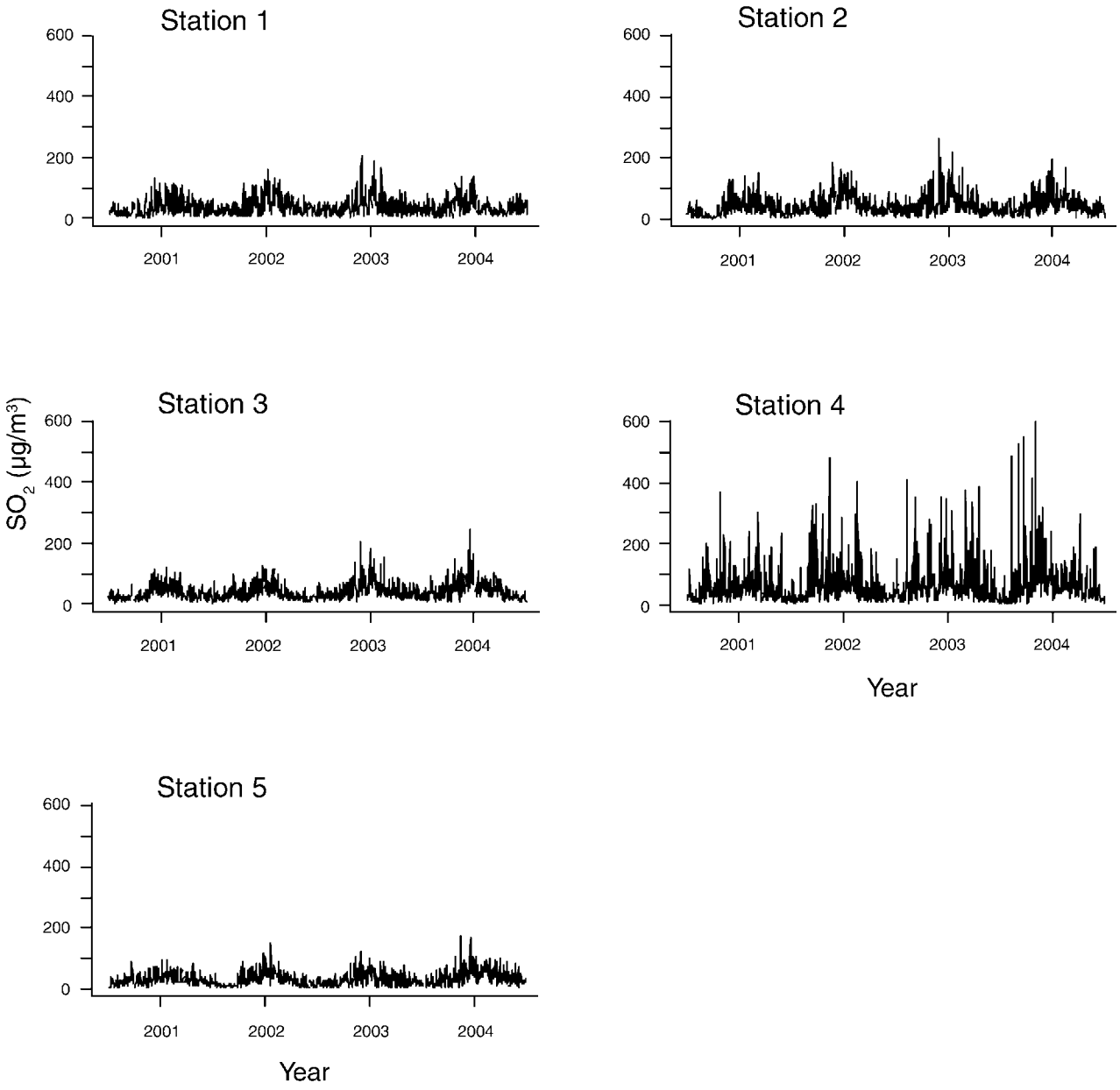

Figure D.3. Time-series plots of SO_2 concentrations by monitor.

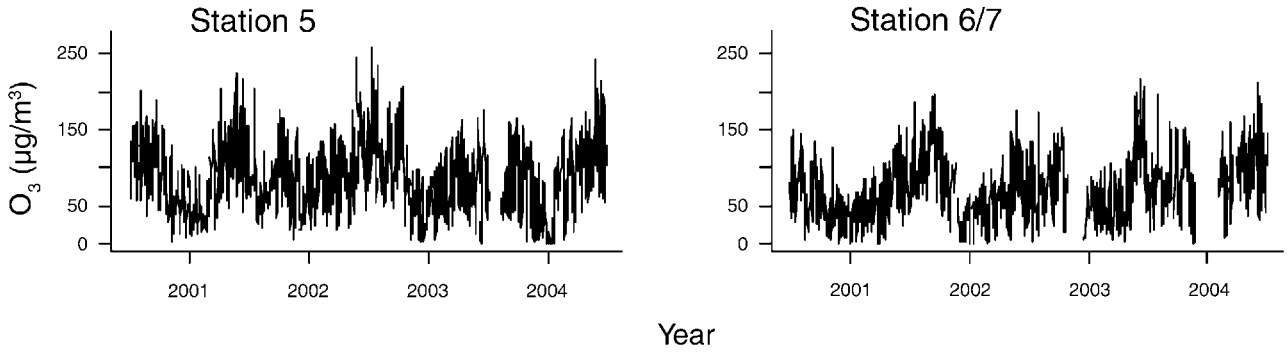

Figure D.4. Time-series plots of O_3 concentrations by monitor.

APPENDIX E. Further Sensitivity Analyses

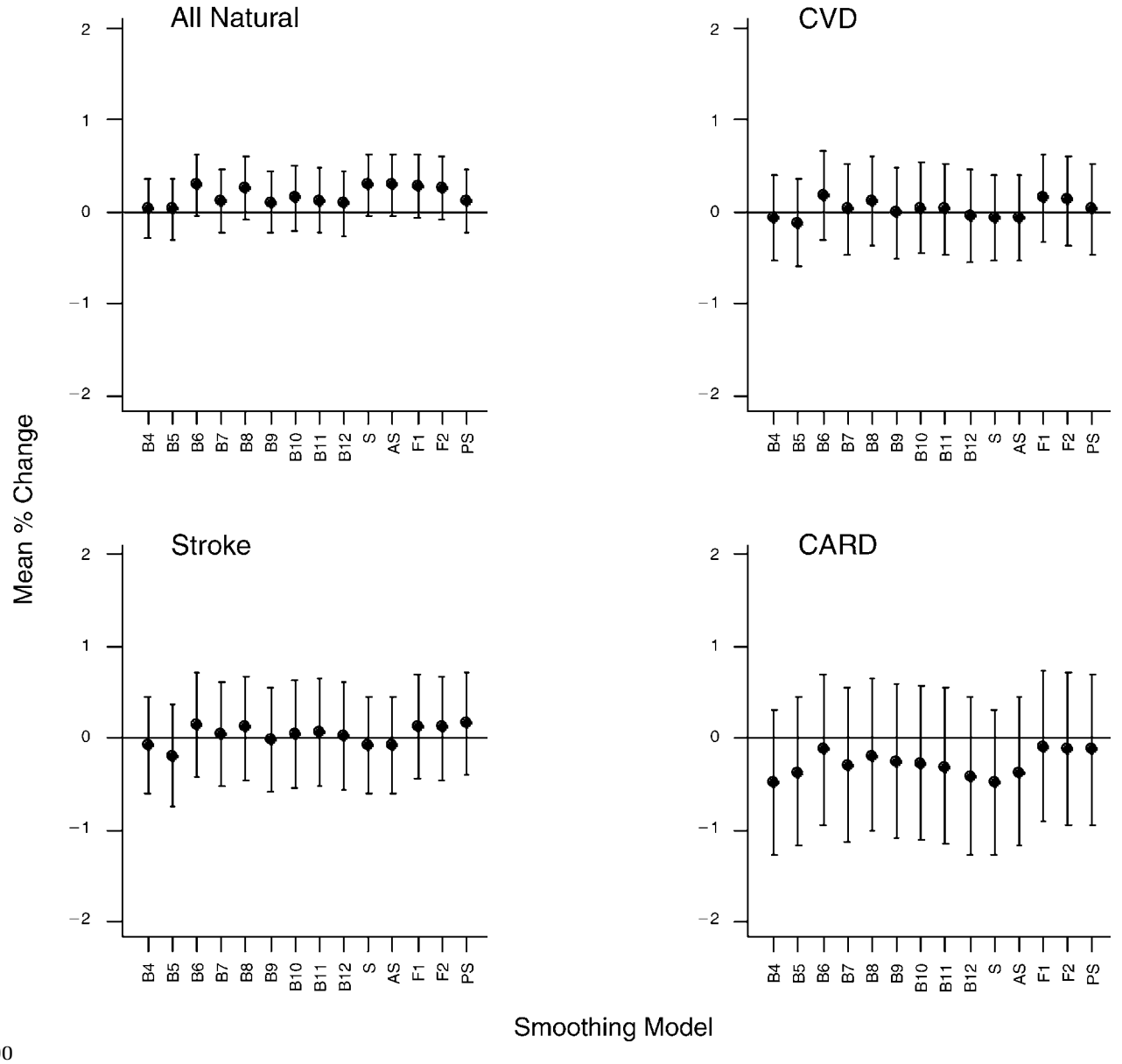

Figure E.1 (*See caption next page*).

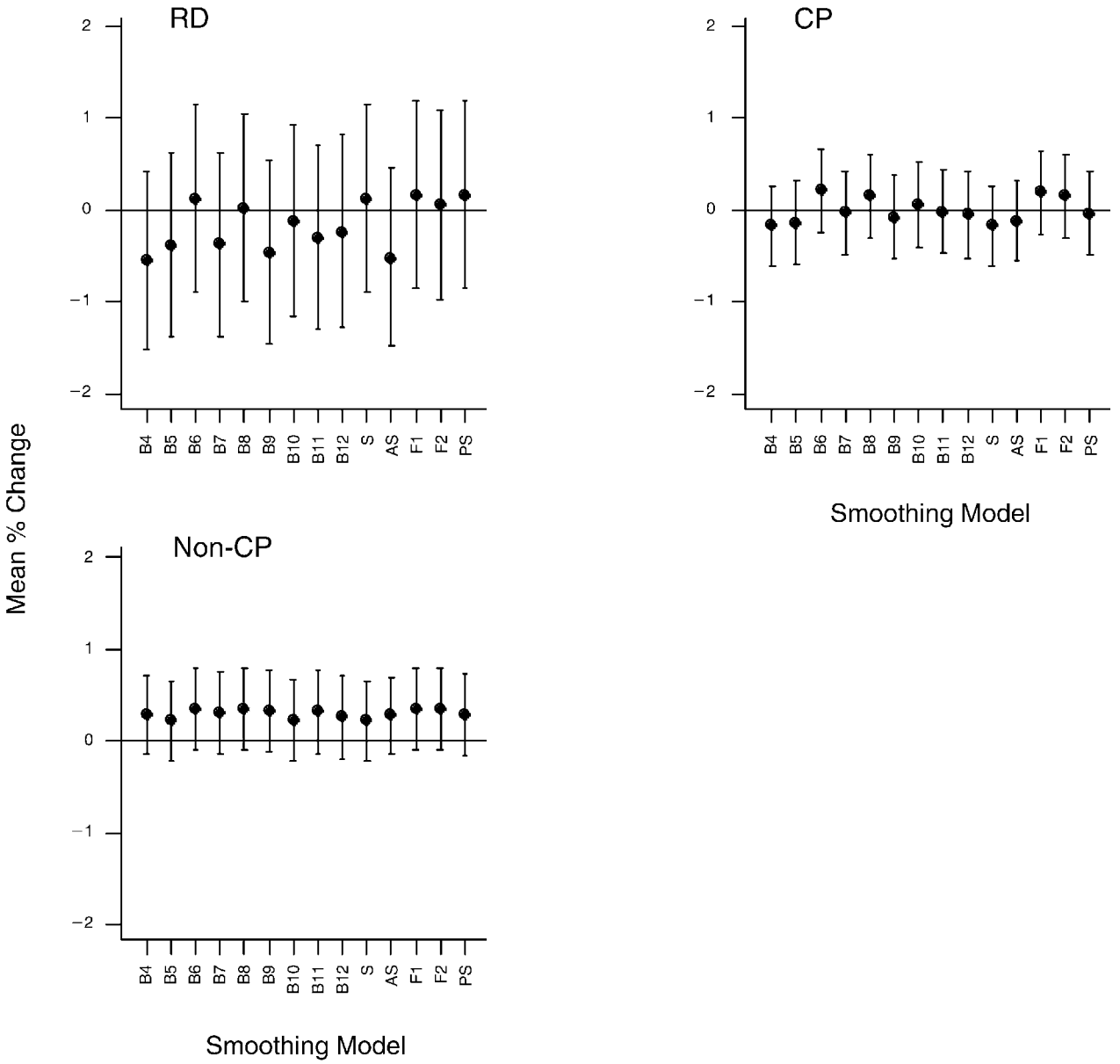

Figure E.1. Sensitivity analysis for different smoothing approaches for O_3 at lag 0–1 day by cause of mortality. B4–B12 indicate the best model with increasing degrees of freedom for the time smoothing function; S indicates the sequential method final model; AS indicates the alternate sequential method final model; F1 indicates the natural spline model 1 with fixed degrees of freedom; F2 indicates the natural spline model 2 with fixed degrees of freedom; and PS indicates the penalized spline method final model.

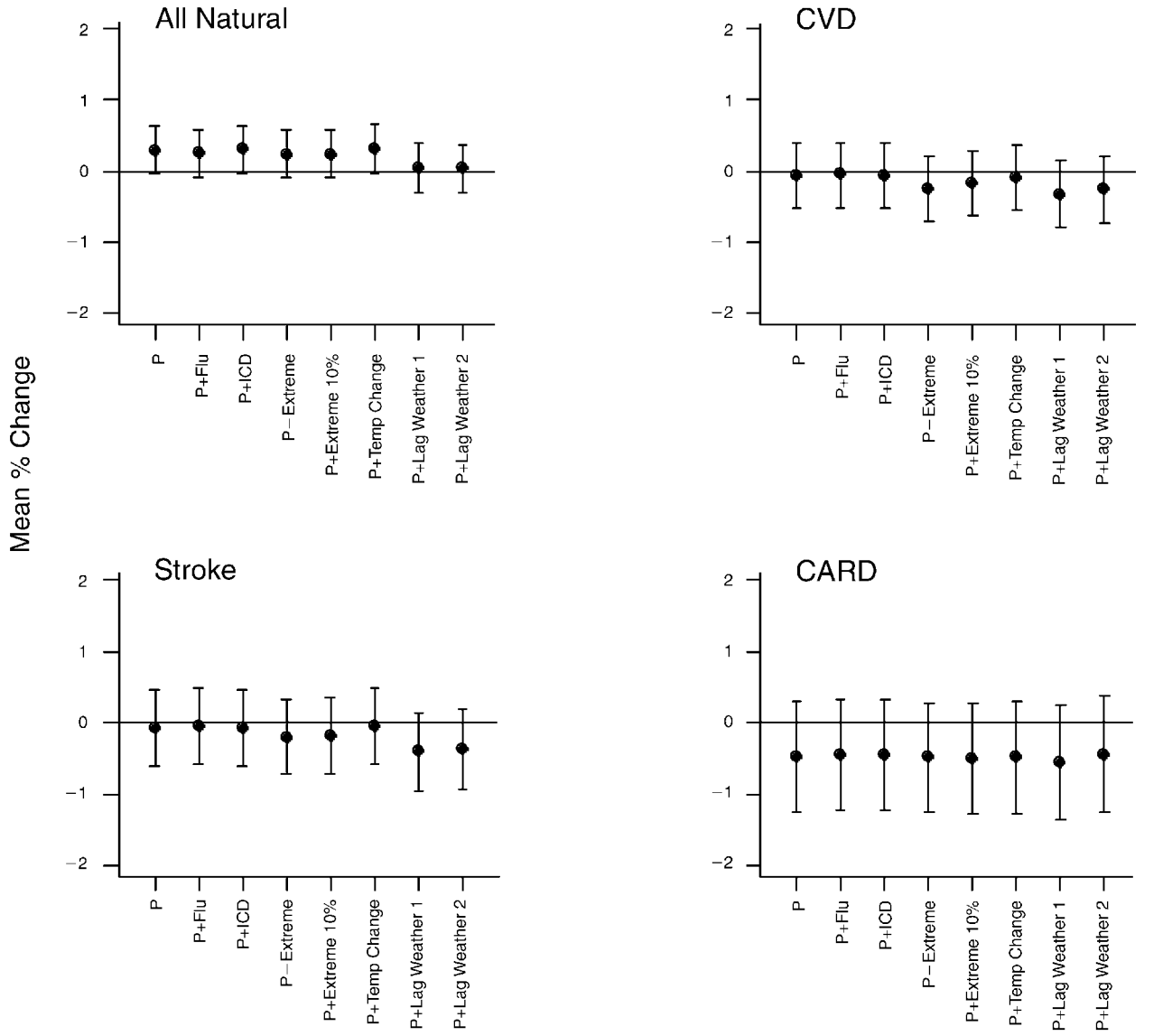

Figure E.2. Sensitivity analysis for different model specifications for O_3 at lag 0–1 day by cause of mortality. P indicates primary model; P+Flu indicates adding flu season; P+ICD indicates adding ICD indicator; P−Extreme indicates excluding extreme weather indicators; P+Extreme 10% indicates using extreme weather indicators based on 10th percentile; P+Temp Change indicates adding daily temperature change (high − low); P+Lag Weather 1 indicates adding the lag 1–2 day mean for weather terms; and P+Lag Weather 2 indicates adding lag 1–2 day mean and lag 3–7 day mean for weather terms.

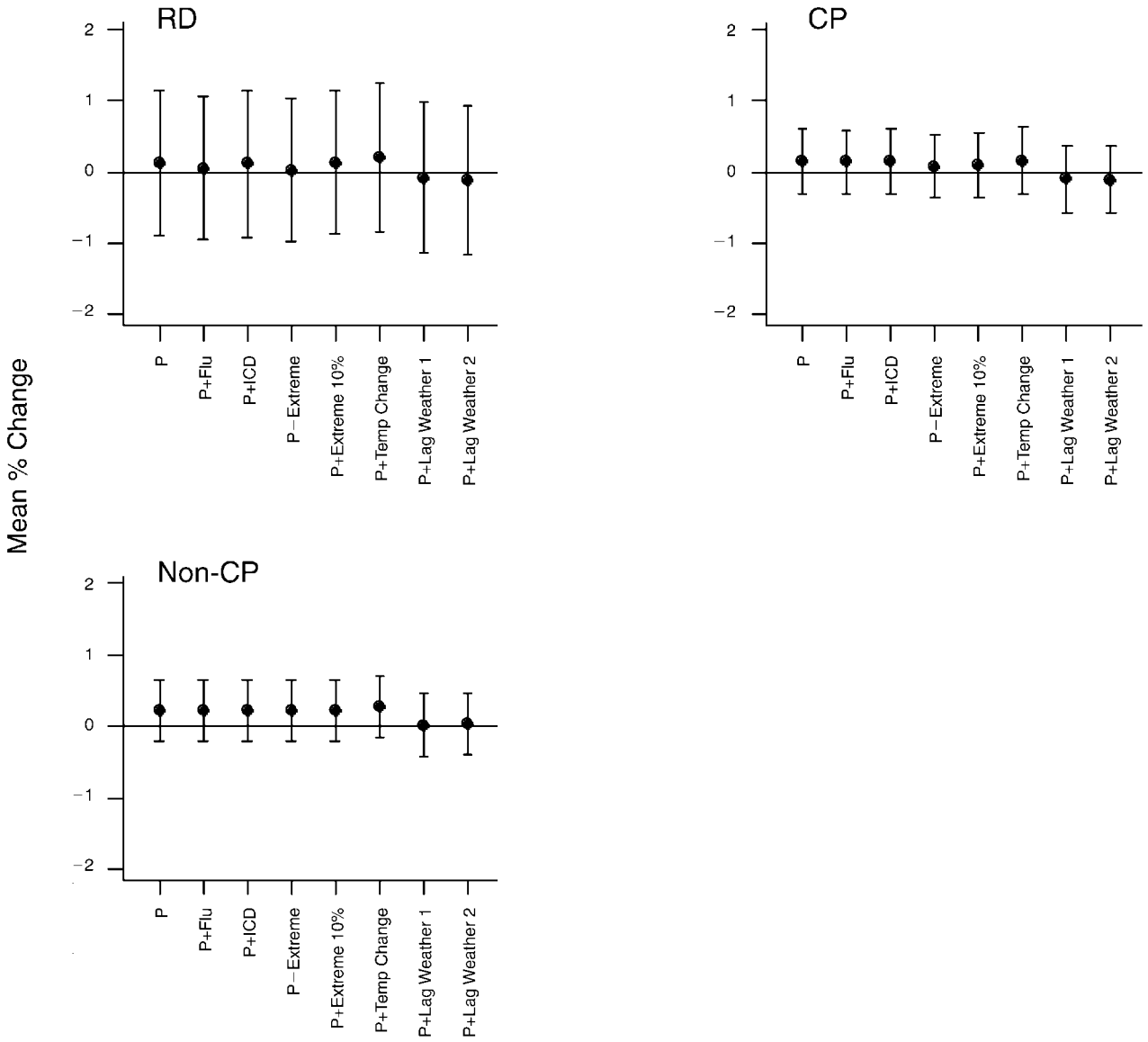

Figure E.2 (*Continued*).

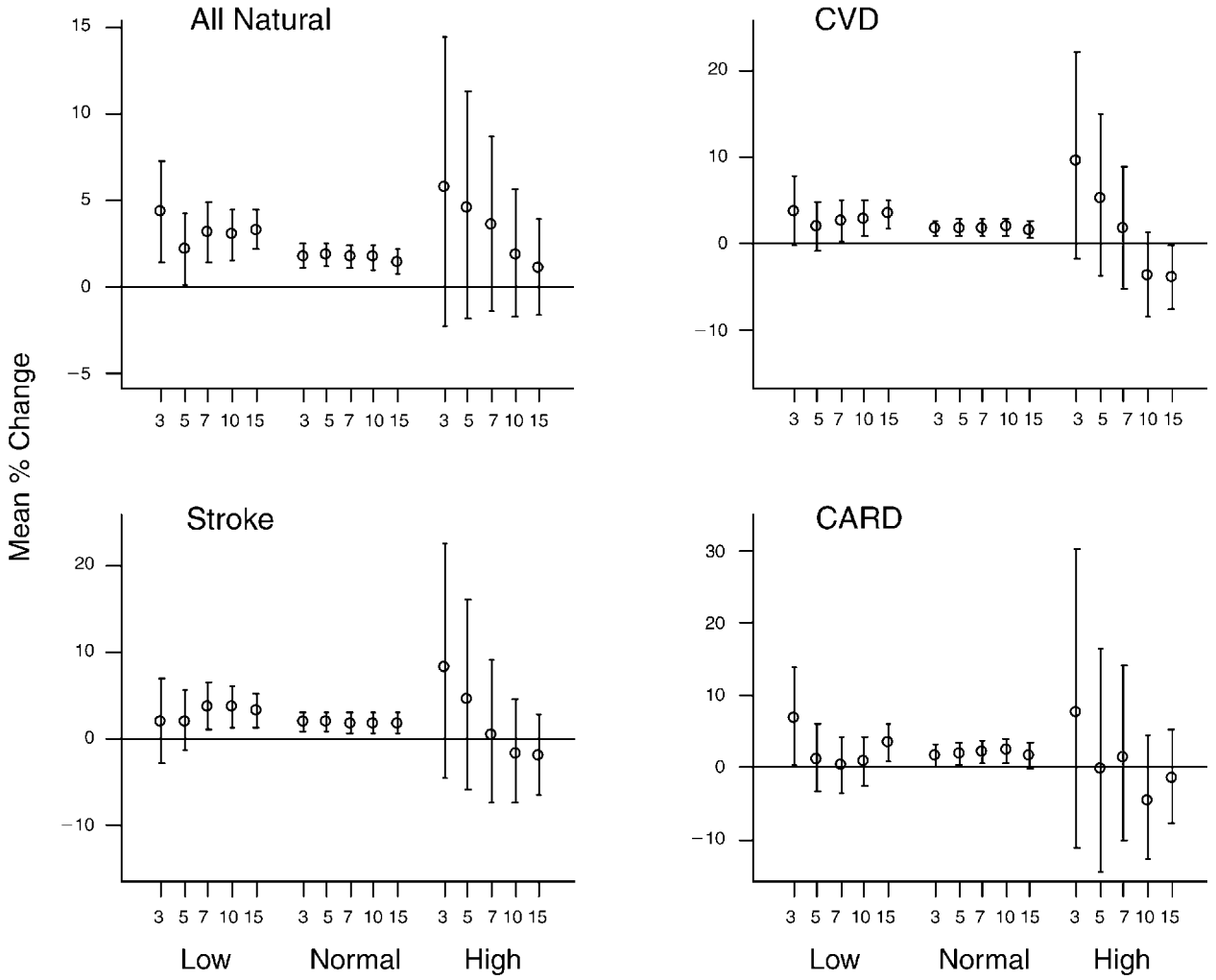

Figure E.3. Mortality plots for NO_2 by cause of death, stratified by varying percentiles of temperature cut-off points at lag 0–1 day. The labels 3, 5, 7, 10, and 15 indicate percentiles used to construct the temperature groups; "low" indicates low temperature that is < each respective percentile; "normal" indicates normal temperature that is ≥ the lower respective percentile and ≤ the upper respective percentile; and "high" indicates high temperature that is > the upper respective percentile.

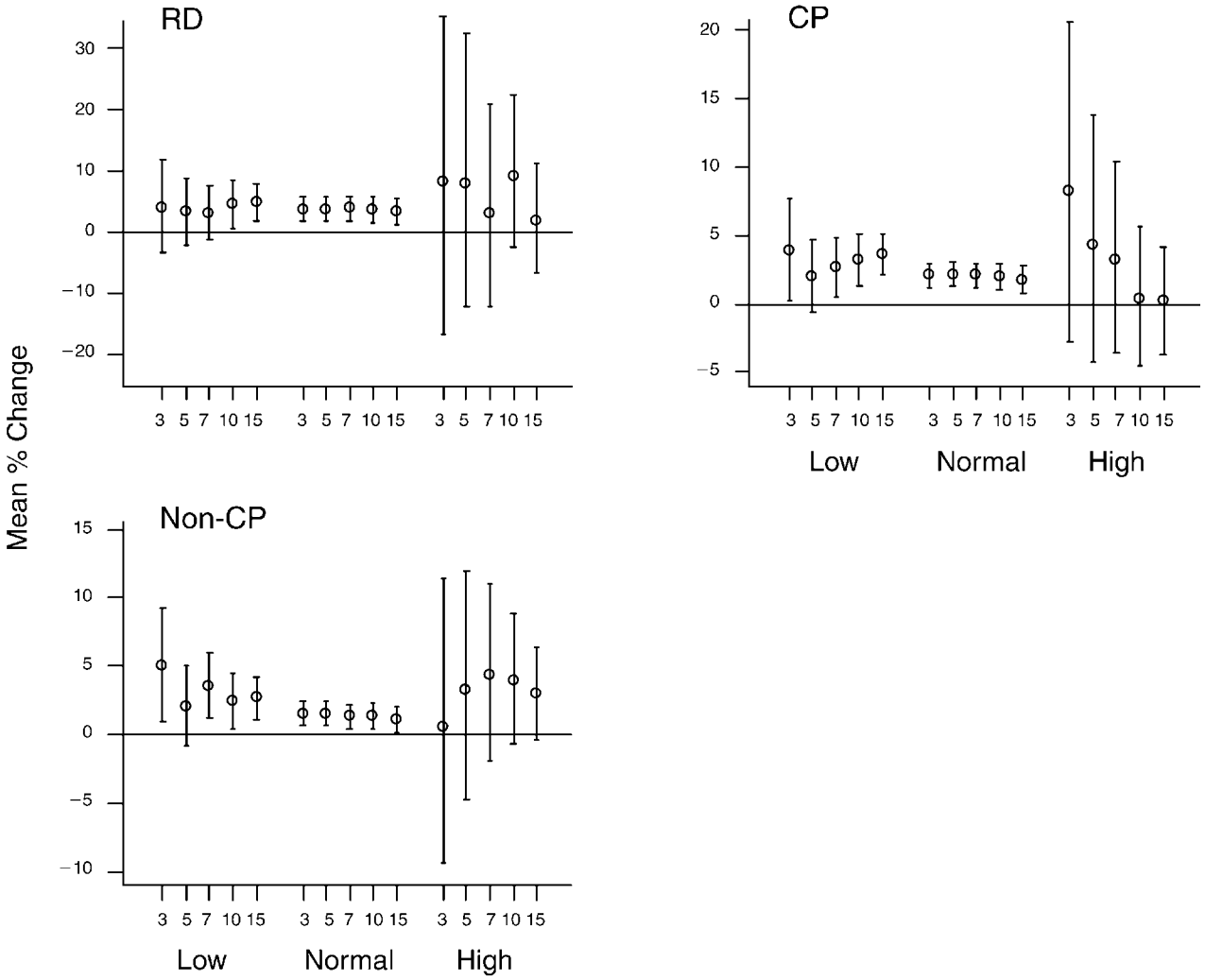

Figure E.3 (*Continued*).

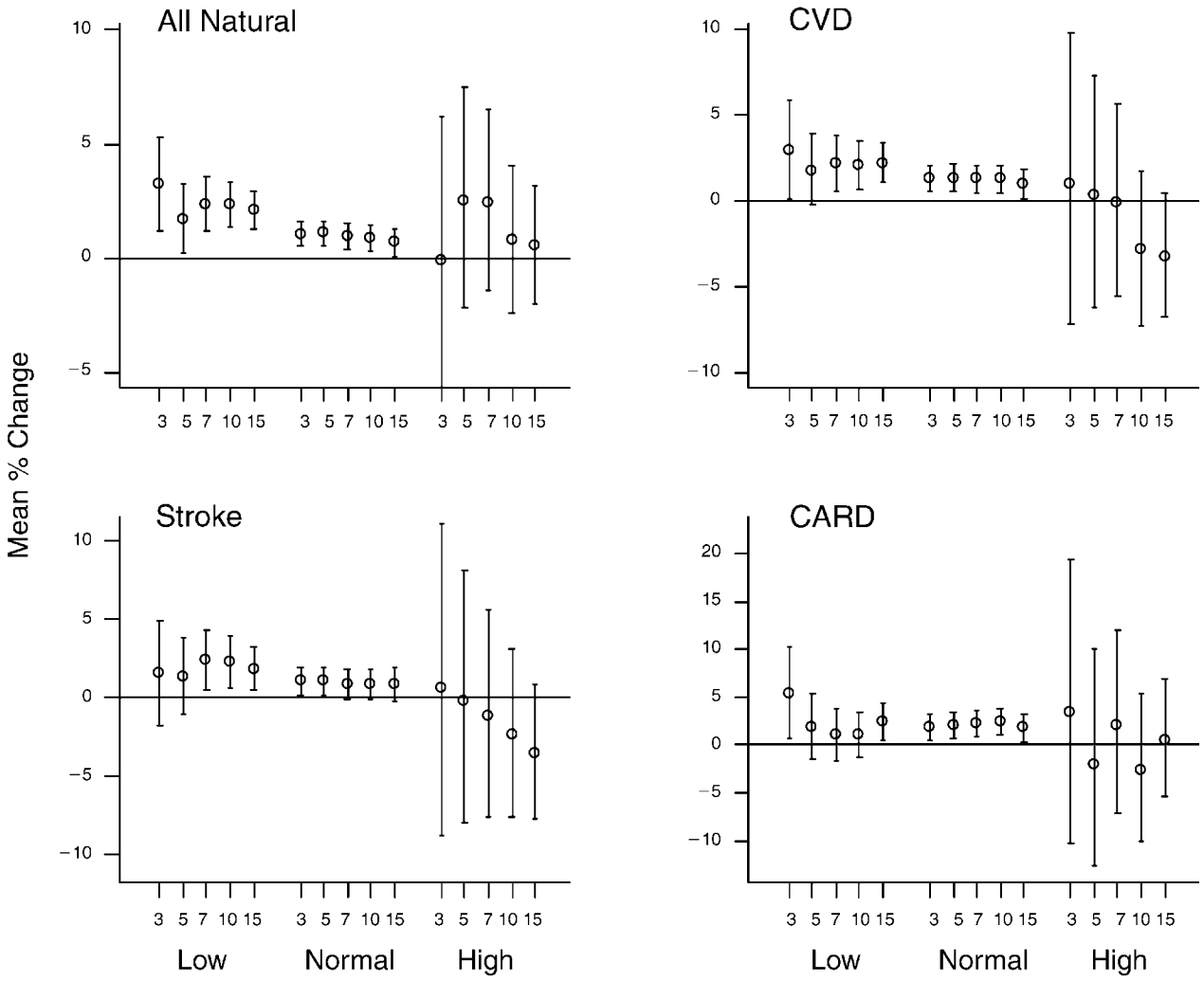

Figure E.4. Mortality plots for SO_2 by cause of death, stratified by varying percentiles of temperature cut-off points at lag 0–1 day. The labels 3, 5, 7, 10, and 15 indicate percentiles used to construct the temperature groups; "low" indicates low temperature that is < each respective percentile; "normal" indicates normal temperature that is ≥ the lower respective percentile and ≤ the upper respective percentile; and "high" indicates high temperature that is > the upper respective percentile.

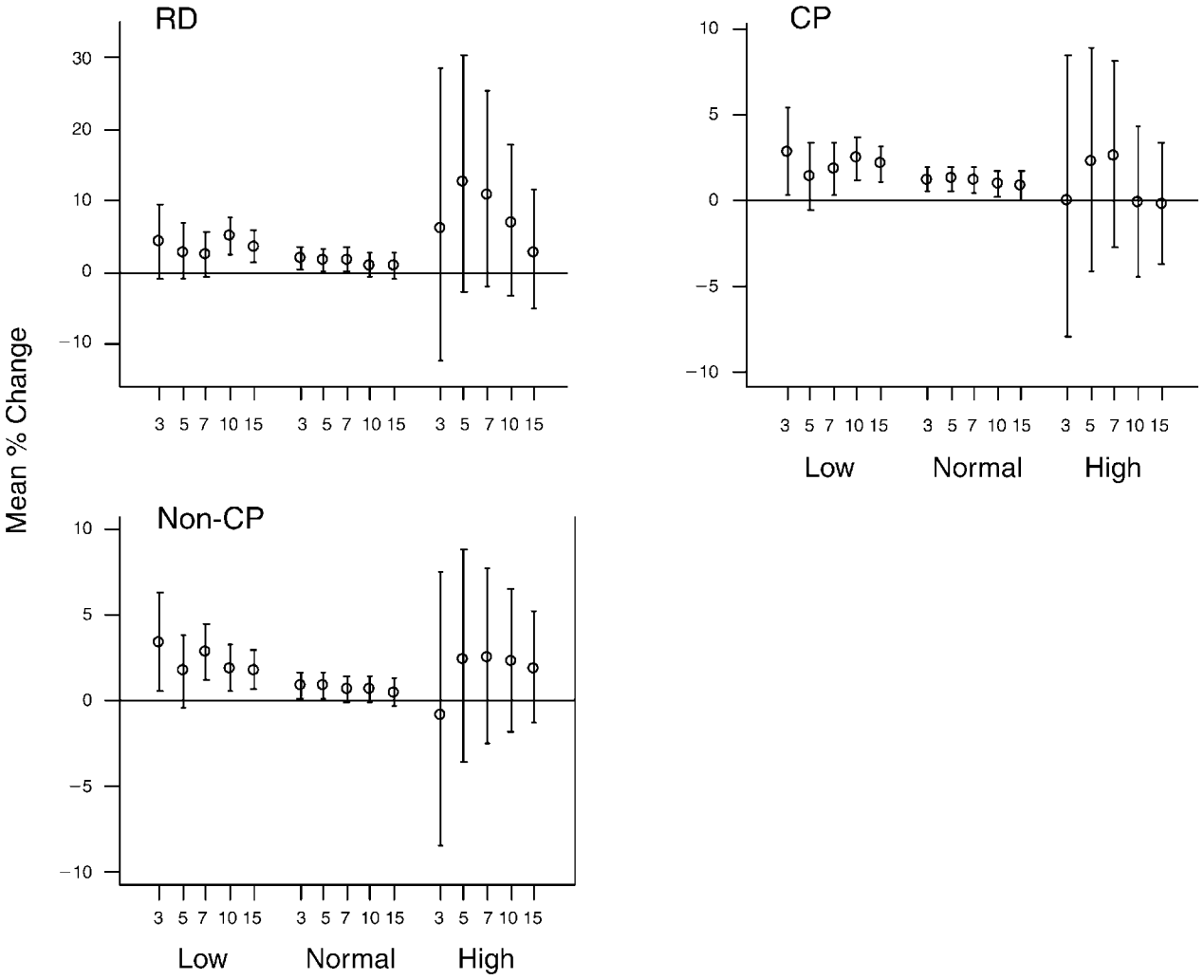

Figure E.4 (*Continued*).

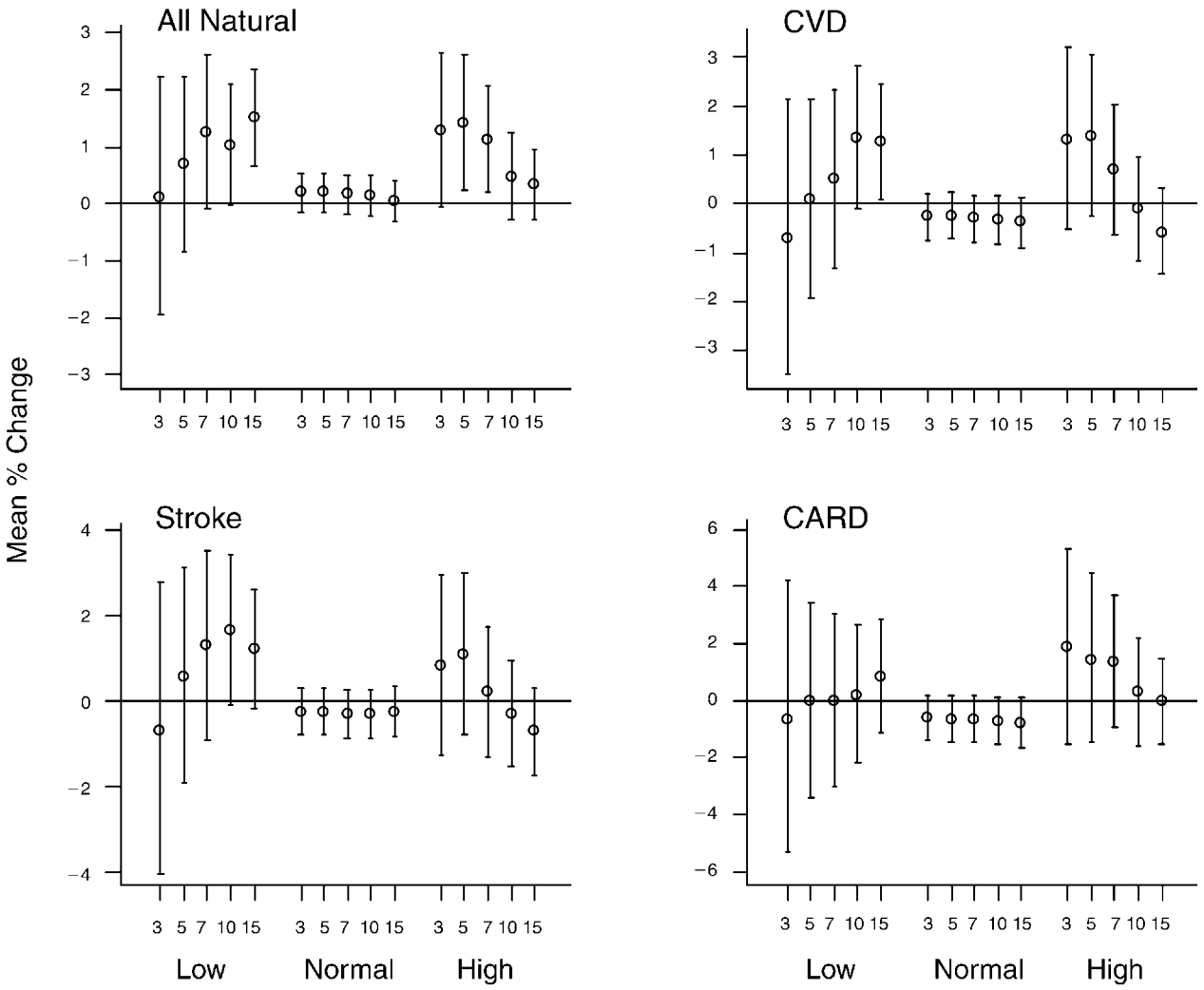

Figure E.5. Mortality plots for O_3 by cause of death, stratified by varying percentiles of temperature cut-off points at lag 0–1 day. The labels 3, 5, 7, 10, and 15 indicate percentiles used to construct the temperature groups; "low" indicates low temperature that is < each respective percentile; "normal" indicates normal temperature that is ≥ the lower respective percentile and ≤ the upper respective percentile; and "high" indicates high temperature that is > the upper respective percentile.

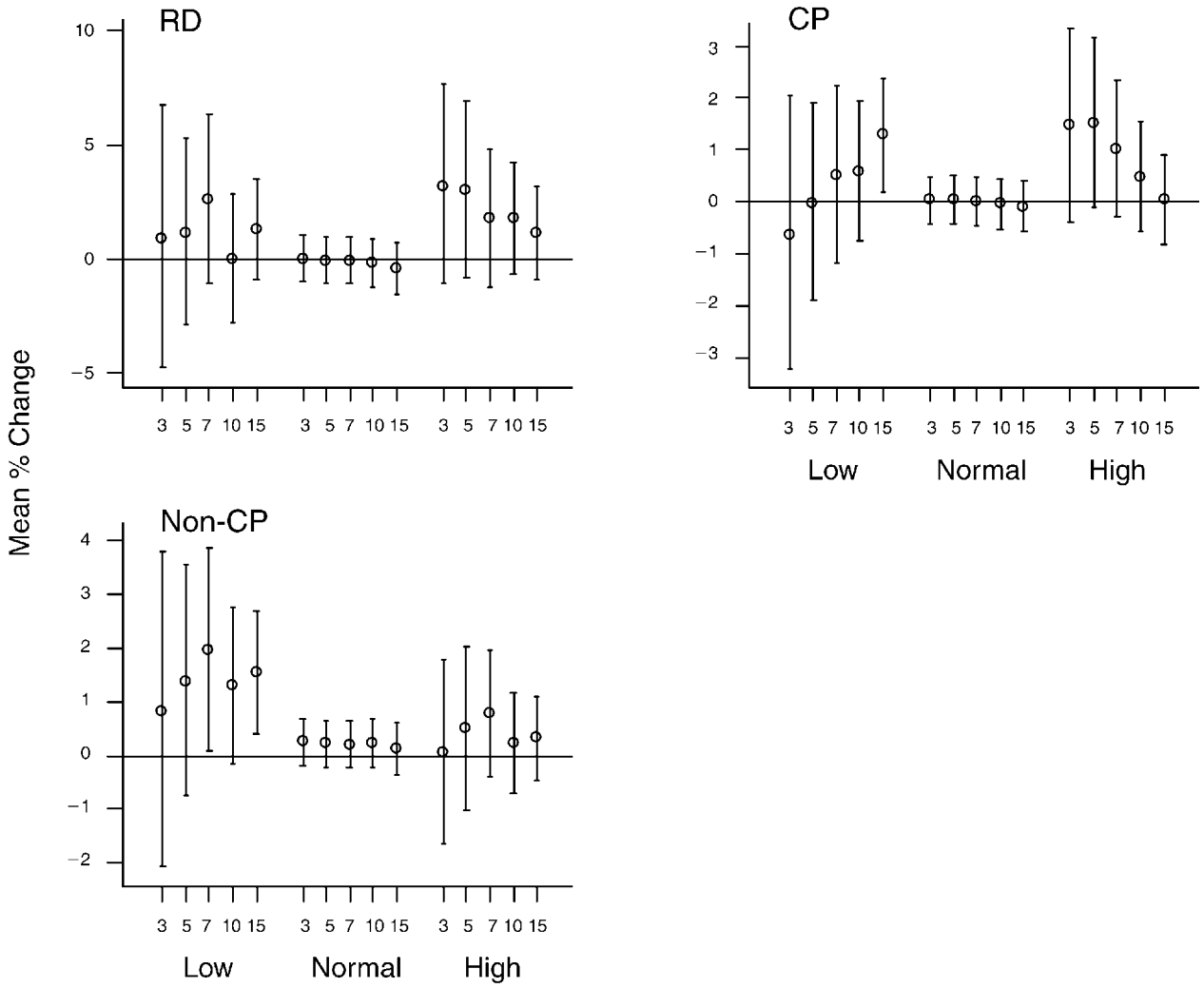

Figure E.5 (*Continued*).

Table E.1. Mean Percentage Change in Daily Cause-Specific Mortality, Evaluated at Different Lags, July 1, 2000, to June 30, 2004

	PM_{10}	NO_2	SO_2	O_3
Cause of Death[a] / Lag	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural				
Lag 0 day	0.36 (0.19 to 0.53)	1.49 (0.93 to 2.04)	0.81 (0.37 to 1.25)	0.13 (−0.15 to 0.42)
Lag 1 day	0.28 (0.12 to 0.44)	1.44 (0.85 to 2.03)	0.70 (0.27 to 1.12)	0.24 (−0.03 to 0.50)
Lag 2 day	−0.05 (−0.20 to 0.10)	0.41 (−0.14 to 0.97)	0.01 (−0.38 to 0.40)	0.20 (−0.03 to 0.44)
Lag 3 day	−0.13 (−0.27 to 0.01)	0.08 (−0.44 to 0.60)	−0.10 (−0.47 to 0.28)	0.01 (−0.21 to 0.24)
Lag 4 day	−0.17 (−0.31 to −0.03)	−0.32 (−0.82 to 0.18)	−0.29 (−0.66 to 0.08)	−0.10 (−0.32 to 0.12)
2-day mean	0.43 (0.24 to 0.62)	1.96 (1.30 to 2.62)	1.20 (0.66 to 1.74)	0.29 (−0.05 to 0.63)
4-day mean	0.08 (−0.14 to 0.31)	1.38 (0.53 to 2.24)	0.61 (−0.08 to 1.31)	0.11 (−0.29 to 0.52)
Cardiovascular				
Lag 0 day	0.51 (0.27 to 0.74)	1.61 (0.82 to 2.41)	0.80 (0.17 to 1.43)	−0.19 (−0.57 to 0.19)
Lag 1 day	0.36 (0.13 to 0.58)	1.52 (0.69 to 2.36)	1.03 (0.43 to 1.64)	0.02 (−0.34 to 0.38)
Lag 2 day	0.06 (−0.15 to 0.27)	0.63 (−0.15 to 1.41)	0.21 (−0.35 to 0.77)	0.07 (−0.25 to 0.39)
Lag 3 day	0.00 (−0.20 to 0.21)	0.46 (−0.27 to 1.20)	0.00 (−0.53 to 0.54)	−0.10 (−0.41 to 0.21)
Lag 4 day	−0.03 (−0.23 to 0.16)	0.09 (−0.62 to 0.80)	−0.33 (−0.86 to 0.20)	−0.30 (−0.61 to 0.00)
2-day mean	0.57 (0.31 to 0.84)	2.12 (1.18 to 3.06)	1.47 (0.70 to 2.25)	−0.07 (−0.53 to 0.39)
4-day mean	0.36 (0.06 to 0.67)	2.07 (0.91 to 3.25)	1.01 (0.03 to 2.01)	−0.27 (−0.81 to 0.28)
Stroke				
Lag 0 day	0.43 (0.15 to 0.71)	1.44 (0.50 to 2.38)	0.43 (−0.31 to 1.18)	−0.38 (−0.83 to 0.07)
Lag 1 day	0.40 (0.13 to 0.67)	1.75 (0.77 to 2.74)	0.91 (0.20 to 1.63)	0.19 (−0.23 to 0.61)
Lag 2 day	0.21 (−0.04 to 0.46)	0.89 (−0.03 to 1.81)	0.21 (−0.44 to 0.87)	0.10 (−0.28 to 0.48)
Lag 3 day	0.00 (−0.24 to 0.24)	0.69 (−0.17 to 1.56)	0.11 (−0.52 to 0.75)	−0.15 (−0.52 to 0.21)
Lag 4 day	−0.05 (−0.28 to 0.18)	0.07 (−0.76 to 0.91)	−0.36 (−0.98 to 0.27)	−0.45 (−0.80 to −0.09)
2-day mean	0.57 (0.25 to 0.88)	2.17 (1.07 to 3.28)	1.10 (0.19 to 2.02)	−0.08 (−0.61 to 0.45)
4-day mean	0.44 (0.08 to 0.80)	2.31 (0.94 to 3.70)	0.83 (−0.33 to 2.00)	−0.49 (−1.13 to 0.14)
Cardiac				
Lag 0 day	0.48 (0.07 to 0.88)	1.73 (0.40 to 3.09)	1.19 (0.13 to 2.26)	−0.22 (−0.88 to 0.44)
Lag 1 day	0.29 (−0.10 to 0.68)	1.30 (−0.11 to 2.73)	1.40 (0.38 to 2.43)	−0.45 (−1.07 to 0.17)
Lag 2 day	−0.22 (−0.58 to 0.14)	0.22 (−1.09 to 1.55)	−0.02 (−0.95 to 0.93)	−0.06 (−0.61 to 0.51)
Lag 3 day	0.04 (−0.30 to 0.39)	−0.14 (−1.38 to 1.10)	−0.40 (−1.30 to 0.51)	−0.19 (−0.72 to 0.34)
Lag 4 day	0.07 (−0.26 to 0.41)	0.38 (−0.81 to 1.59)	−0.12 (−1.01 to 0.77)	−0.09 (−0.61 to 0.43)
2-day mean	0.49 (0.04 to 0.94)	2.02 (0.44 to 3.62)	2.04 (0.74 to 3.37)	−0.48 (−1.26 to 0.30)
4-day mean	0.24 (−0.28 to 0.76)	1.68 (−0.28 to 3.66)	1.06 (−0.59 to 2.74)	−0.25 (−1.18 to 0.68)

Table continues next page

[a] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table E.1 (*Continued*). Mean Percentage Change in Daily Cause-Specific Mortality, Evaluated at Different Lags, July 1, 2000, to June 30, 2004

	PM_{10}	NO_2	SO_2	O_3
Cause of Death[a] / Lag	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
Respiratory				
Lag 0 day	0.77 (0.29 to 1.24)	2.79 (1.19 to 4.42)	2.20 (0.99 to 3.42)	0.37 (−0.48 to 1.23)
Lag 1 day	0.61 (0.14 to 1.07)	2.84 (1.13 to 4.58)	0.50 (−0.68 to 1.70)	−0.18 (−0.97 to 0.62)
Lag 2 day	−0.04 (−0.46 to 0.39)	1.04 (−0.53 to 2.63)	0.16 (−0.93 to 1.25)	0.22 (−0.50 to 0.94)
Lag 3 day	−0.18 (−0.59 to 0.22)	0.86 (−0.61 to 2.35)	0.54 (−0.50 to 1.59)	0.00 (−0.68 to 0.69)
Lag 4 day	−0.17 (−0.56 to 0.22)	−0.05 (−1.46 to 1.38)	0.68 (−0.35 to 1.72)	0.25 (−0.42 to 0.94)
2-day mean	0.87 (0.34 to 1.41)	3.69 (1.78 to 5.64)	2.10 (0.58 to 3.63)	0.12 (−0.89 to 1.15)
4-day mean	0.30 (−0.33 to 0.93)	3.32 (0.92 to 5.78)	2.53 (0.59 to 4.50)	0.13 (−1.10 to 1.37)
Cardiopulmonary				
Lag 0 day	0.46 (0.24 to 0.68)	1.70 (0.96 to 2.43)	0.95 (0.38 to 1.53)	0.07 (−0.30 to 0.45)
Lag 1 day	0.33 (0.11 to 0.54)	1.53 (0.75 to 2.31)	0.73 (0.18 to 1.28)	0.12 (−0.23 to 0.47)
Lag 2 day	−0.02 (−0.22 to 0.18)	0.51 (−0.21 to 1.24)	0.06 (−0.45 to 0.57)	0.19 (−0.12 to 0.50)
Lag 3 day	−0.09 (−0.28 to 0.09)	0.40 (−0.28 to 1.08)	0.06 (−0.43 to 0.55)	−0.02 (−0.32 to 0.28)
Lag 4 day	−0.13 (−0.31 to 0.05)	−0.18 (−0.84 to 0.47)	−0.21 (−0.69 to 0.28)	−0.16 (−0.45 to 0.14)
2-day mean	0.52 (0.27 to 0.77)	2.17 (1.29 to 3.05)	1.33 (0.62 to 2.05)	0.15 (−0.30 to 0.61)
4-day mean	0.13 (−0.16 to 0.43)	1.71 (0.58 to 2.85)	0.83 (−0.08 to 1.74)	−0.10 (−0.65 to 0.45)
Non-cardiopulmonary				
Lag 0 day	0.24 (0.02 to 0.46)	1.18 (0.44 to 1.92)	0.63 (0.04 to 1.22)	0.07 (−0.29 to 0.43)
Lag 1 day	0.23 (0.02 to 0.44)	1.35 (0.58 to 2.13)	0.67 (0.11 to 1.24)	0.23 (−0.11 to 0.56)
Lag 2 day	−0.07 (−0.27 to 0.13)	0.33 (−0.39 to 1.07)	−0.04 (−0.56 to 0.49)	0.09 (−0.21 to 0.39)
Lag 3 day	−0.16 (−0.35 to 0.03)	−0.28 (−0.97 to 0.42)	−0.30 (−0.81 to 0.21)	−0.07 (−0.35 to 0.22)
Lag 4 day	−0.20 (−0.39 to −0.02)	−0.39 (−1.06 to 0.28)	−0.36 (−0.86 to 0.14)	−0.16 (−0.44 to 0.12)
2-day mean	0.30 (0.05 to 0.54)	1.66 (0.79 to 2.53)	1.01 (0.29 to 1.73)	0.22 (−0.21 to 0.65)
4-day mean	−0.06 (−0.35 to 0.24)	0.79 (−0.30 to 1.90)	0.13 (−0.78 to 1.05)	0.07 (−0.43 to 0.58)

[a] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table E.2. Two-Pollutant Regression Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in O_3 Concentration, for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a]

Cause of Death[b] / Pollutant(s)	Mean % Change (95% CI)
All natural	
O_3	0.29 (−0.05 to 0.63)
O_3 + PM_{10}	0.24 (−0.10 to 0.58)
O_3 + NO_2	0.10 (−0.24 to 0.44)
O_3 + SO_2	0.16 (−0.19 to 0.50)
Cardiovascular	
O_3	−0.07 (−0.53 to 0.39)
O_3 + PM_{10}	−0.09 (−0.55 to 0.36)
O_3 + NO_2	−0.23 (−0.69 to 0.23)
O_3 + SO_2	−0.18 (−0.64 to 0.28)
Stroke	
O_3	−0.08 (−0.61 to 0.45)
O_3 + PM_{10}	−0.12 (−0.65 to 0.41)
O_3 + NO_2	−0.25 (−0.78 to 0.29)
O_3 + SO_2	−0.17 (−0.71 to 0.37)
Cardiac	
O_3	−0.48 (−1.26 to 0.30)
O_3 + PM_{10}	−0.47 (−1.24 to 0.31)
O_3 + NO_2	−0.62 (−1.40 to 0.17)
O_3 + SO_2	−0.64 (−1.42 to 0.15)
Respiratory	
O_3	0.12 (−0.89 to 1.15)
O_3 + PM_{10}	0.08 (−0.93 to 1.10)
O_3 + NO_2	−0.23 (−1.25 to 0.80)
O_3 + SO_2	−0.10 (−1.13 to 0.94)
Cardiopulmonary	
O_3	0.15 (−0.30 to 0.61)
O_3 + PM_{10}	0.09 (−0.36 to 0.55)
O_3 + NO_2	−0.07 (−0.53 to 0.39)
O_3 + SO_2	−0.01 (−0.47 to 0.45)
Non-cardiopulmonary	
O_3	0.22 (−0.21 to 0.65)
O_3 + PM_{10}	0.20 (−0.23 to 0.63)
O_3 + NO_2	0.08 (−0.35 to 0.51)
O_3 + SO_2	0.13 (−0.30 to 0.56)

[a] The covariates considered in the GAM are indicators of days of the week; two peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothing functions for time, daily mean temperature, and daily mean RH; and local smoothing over two peaks of mortality and the remaining period.

[b] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table E.3. Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in Concentrations of Pollutants by Cause of Death and Temperature, for Lag 0–1 Day, Without Indicators for Season, July 1, 2000, to June 30, 2004[a,b]

	Temperature			
	Normal	Low	High	
Cause of Death[c] / Pollutant	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)	*P* Value[d]
All natural				
PM_{10}	0.39 (0.20 to 0.58)	0.64 (−0.08 to 1.36)	2.22 (0.77 to 3.70)	0.014
NO_2	1.92 (1.25 to 2.59)	2.25 (0.19 to 4.36)	4.65 (−1.73 to 11.45)	0.603
SO_2	1.14 (0.59 to 1.70)	1.78 (0.28 to 3.30)	2.45 (−3.26 to 6.03)	0.528
O_3	0.23 (−0.12 to 0.57)	0.69 (−0.82 to 2.22)	1.43 (0.25 to 2.62)	0.056
Cardiovascular				
PM_{10}	0.52 (0.25 to 0.79)	0.89 (−0.08 to 1.88)	3.42 (1.37 to 5.52)	0.006
NO_2	2.06 (1.11 to 3.02)	2.46 (−0.39 to 5.39)	5.59 (−3.45 to 15.48)	0.676
SO_2	1.43 (0.63 to 2.23)	2.18 (0.10 to 4.30)	0.38 (−6.20 to 7.41)	0.684
O_3	−0.16 (−0.63 to 0.30)	0.25 (−1.79 to 2.35)	1.44 (−0.21 to 3.12)	0.098
Stroke				
PM_{10}	0.52 (0.21 to 0.84)	0.88 (−0.30 to 2.07)	2.55 (0.17 to 5.00)	0.190
NO_2	2.12 (0.99 to 3.25)	2.55 (−0.85 to 6.06)	4.93 (−5.56 to 16.59)	0.843
SO_2	1.07 (0.14 to 2.01)	1.68 (−0.78 to 4.20)	−0.21 (−8.00 to 8.23)	0.833
O_3	−0.17 (−0.71 to 0.38)	0.58 (−1.92 to 3.13)	1.20 (−0.66 to 3.11)	0.283
Cardiac				
PM_{10}	0.44 (−0.02 to 0.89)	0.65 (−0.96 to 2.28)	3.49 (−0.05 to 7.15)	0.213
NO_2	2.07 (0.46 to 3.71)	1.52 (−3.11 to 6.37)	−0.04 (−14.38 to 16.70)	0.937
SO_2	2.08 (0.74 to 3.45)	2.18 (−1.22 to 5.69)	−2.15 (−12.80 to 9.79)	0.748
O_3	−0.59 (−1.38 to 0.20)	0.10 (−3.25 to 3.58)	1.46 (−1.46 to 4.47)	0.337
Respiratory				
PM_{10}	0.86 (0.32 to 1.41)	1.11 (−0.73 to 2.99)	1.12 (−3.56 to 6.03)	0.945
NO_2	3.69 (1.74 to 5.68)	3.26 (−2.05 to 8.86)	7.84 (−12.24 to 32.52)	0.895
SO_2	1.92 (0.37 to 3.49)	2.96 (−0.87 to 6.95)	12.85 (−2.50 to 30.63)	0.248
O_3	−0.02 (−1.05 to 1.02)	1.18 (−2.84 to 5.37)	2.90 (−0.85 to 6.81)	0.178
Cardiopulmonary				
PM_{10}	0.48 (0.23 to 0.73)	0.67 (−0.25 to 1.60)	3.23 (1.23 to 5.27)	0.008
NO_2	2.16 (1.27 to 3.06)	1.88 (−0.76 to 4.59)	4.62 (−4.09 to 14.12)	0.803
SO_2	1.32 (0.60 to 2.06)	1.34 (−0.57 to 3.28)	1.81 (−4.50 to 8.53)	0.986
O_3	0.08 (−0.38 to 0.55)	0.01 (−1.89 to 1.94)	1.58 (−0.05 to 3.24)	0.117
Non-cardiopulmonary				
PM_{10}	0.28 (0.03 to 0.53)	0.42 (−0.58 to 1.43)	0.87 (−1.00 to 2.78)	0.802
NO_2	1.60 (0.72 to 2.49)	2.38 (−0.50 to 5.35)	3.27 (−4.77 to 12.00)	0.809
SO_2	0.92 (0.18 to 1.67)	1.86 (−0.23 to 4.01)	2.61 (−3.40 to 9.00)	0.595
O_3	0.19 (−0.24 to 0.63)	1.40 (−0.73 to 3.58)	0.44 (−1.06 to 1.96)	0.502

[a] Normal temperature = between 5th and 95th percentile; low temperature < 5th percentile; and high temperature > 95th percentile.

[b] Estimates were obtained from the main effect and pollutant × temperature interaction models. The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothing functions for time, daily mean temperature, and daily mean RH; and local smoothing over 2 peaks of mortality and the remaining period (without indicators for season).

[c] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

[d] For the interaction terms.

Table E.4. Copollutant Regression Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in NO_2 Concentration by Temperature, for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a,b]

	Temperature		
	Normal	Low	High
Cause of Death[c] / Pollutant(s)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural			
NO_2	1.89 (1.22 to 2.57)	2.22 (0.16 to 4.32)	4.59 (−1.78 to 11.36)
$NO_2 + PM_{10}$	1.70 (0.87 to 2.54)	2.05 (−0.06 to 4.19)	4.64 (−1.75 to 11.45)
$NO_2 + SO_2$	1.64 (0.83 to 2.47)	1.90 (−0.24 to 4.08)	4.38 (−1.99 to 11.15)
$NO_2 + O_3$	1.94 (1.22 to 2.67)	2.62 (0.47 to 4.82)	5.01 (−2.49 to 13.10)
Cardiovascular			
NO_2	1.89 (0.95 to 2.84)	2.03 (−0.78 to 4.92)	5.23 (−3.71 to 15.00)
$NO_2 + PM_{10}$	1.57 (0.39 to 2.75)	1.71 (−1.18 to 4.68)	4.74 (−4.21 to 14.53)
$NO_2 + SO_2$	1.42 (0.27 to 2.58)	1.40 (−1.52 to 4.41)	4.88 (−4.04 to 14.63)
$NO_2 + O_3$	2.14 (1.14 to 3.14)	2.79 (−0.15 to 5.81)	6.81 (−3.67 to 18.42)
Stroke			
NO_2	1.94 (0.82 to 3.06)	2.02 (−1.35 to 5.50)	4.42 (−5.96 to 15.95)
$NO_2 + PM_{10}$	1.69 (0.30 to 3.09)	1.78 (−1.67 to 5.35)	4.04 (−6.37 to 15.61)
$NO_2 + SO_2$	1.89 (0.53 to 3.27)	1.96 (−1.56 to 5.60)	4.39 (−6.01 to 15.93)
$NO_2 + O_3$	2.05 (0.88 to 3.22)	2.51 (−0.98 to 6.13)	7.60 (−4.35 to 21.05)
Cardiac			
NO_2	1.92 (0.31 to 3.55)	1.17 (−3.44 to 6.00)	−0.31 (−14.58 to 16.35)
$NO_2 + PM_{10}$	1.78 (−0.23 to 3.83)	1.04 (−3.71 to 6.02)	−0.51 (−14.84 to 16.24)
$NO_2 + SO_2$	0.74 (−1.20 to 2.72)	−0.35 (−5.09 to 4.64)	−1.17 (−15.33 to 15.37)
$NO_2 + O_3$	2.36 (0.65 to 4.09)	2.30 (−2.54 to 7.38)	1.92 (−15.60 to 23.09)
Respiratory			
NO_2	3.64 (1.69 to 5.63)	3.17 (−2.13 to 8.75)	7.68 (−12.36 to 32.30)
$NO_2 + PM_{10}$	2.99 (0.56 to 5.47)	2.56 (−2.86 to 8.29)	5.16 (−14.44 to 29.24)
$NO_2 + SO_2$	3.32 (0.91 to 5.78)	2.76 (−2.79 to 8.63)	7.40 (−12.61 to 32.00)
$NO_2 + O_3$	3.81 (1.74 to 5.92)	3.05 (−2.41 to 8.81)	19.67 (−5.80 to 52.03)
Cardiopulmonary			
NO_2	2.13 (1.24 to 3.03)	1.98 (−0.65 to 4.68)	4.31 (−4.32 to 13.72)
$NO_2 + PM_{10}$	1.75 (0.65 to 2.86)	1.63 (−1.05 to 4.39)	3.70 (−4.94 to 13.12)
$NO_2 + SO_2$	1.82 (0.73 to 2.93)	1.57 (−1.19 to 4.40)	4.08 (−4.55 to 13.48)
$NO_2 + O_3$	2.21 (1.26 to 3.17)	2.36 (−0.34 to 5.14)	7.74 (−2.52 to 19.09)
Non-cardiopulmonary			
NO_2	1.58 (0.69 to 2.47)	2.13 (−0.77 to 5.11)	3.27 (−4.78 to 12.00)
$NO_2 + PM_{10}$	1.59 (0.48 to 2.71)	2.15 (−0.83 to 5.21)	3.54 (−4.57 to 12.34)
$NO_2 + SO_2$	1.44 (0.35 to 2.54)	1.94 (−1.08 to 5.04)	3.16 (−4.90 to 11.90)
$NO_2 + O_3$	1.67 (0.71 to 2.63)	2.59 (−0.47 to 5.76)	0.60 (−8.64 to 10.76)

[a] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

[b] Estimates were obtained from the main effect and pollutant × temperature interaction models. The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothing functions for time, daily mean temperature, and daily mean RH; local smoothing over 2 peaks of mortality and the remaining period; and indicators for season.

[c] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table E.5. Copollutant Regression Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in SO_2 Concentration by Temperature, for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a,b]

	Temperature		
	Normal	Low	High
Cause of Death[c] / Pollutant(s)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural			
SO_2	1.10 (0.55 to 1.66)	1.74 (0.25 to 3.26)	2.56 (−2.11 to 7.45)
$SO_2 + PM_{10}$	0.83 (0.26 to 1.42)	1.47 (−0.03 to 2.99)	2.01 (−2.62 to 6.86)
$SO_2 + NO_2$	0.29 (−0.38 to 0.97)	0.84 (−0.70 to 2.40)	1.96 (−2.67 to 6.82)
$SO_2 + O_3$	1.08 (0.48 to 1.68)	1.99 (0.41 to 3.60)	−0.07 (−6.51 to 6.82)
Cardiovascular			
SO_2	1.36 (0.57 to 2.15)	1.81 (−0.24 to 3.91)	0.35 (−6.18 to 7.32)
$SO_2 + PM_{10}$	1.07 (0.24 to 1.90)	1.48 (−0.58 to 3.59)	0.08 (−6.44 to 7.04)
$SO_2 + NO_2$	0.65 (−0.31 to 1.62)	1.01 (−1.12 to 3.18)	−0.16 (−6.67 to 6.80)
$SO_2 + O_3$	1.51 (0.69 to 2.34)	2.40 (0.24 to 4.61)	−0.63 (−9.51 to 9.11)
Stroke			
SO_2	0.99 (0.06 to 1.92)	1.32 (−1.12 to 3.82)	−0.26 (−8.01 to 8.14)
$SO_2 + PM_{10}$	0.68 (−0.29 to 1.66)	0.97 (−1.48 to 3.48)	−0.53 (−8.26 to 7.86)
$SO_2 + NO_2$	0.06 (−1.07 to 1.20)	0.27 (−2.25 to 2.85)	−0.90 (−8.61 to 7.46)
$SO_2 + O_3$	1.10 (0.14 to 2.07)	1.75 (−0.80 to 4.37)	−1.12 (−11.22 to 10.13)
Cardiac			
SO_2	2.04 (0.70 to 3.39)	1.90 (−1.50 to 5.41)	−1.99 (−12.65 to 9.98)
$SO_2 + PM_{10}$	1.89 (0.48 to 3.32)	1.73 (−1.70 to 5.27)	−2.13 (−12.79 to 9.84)
$SO_2 + NO_2$	1.71 (0.08 to 3.37)	1.52 (−2.02 to 5.20)	−2.22 (−12.89 to 9.75)
$SO_2 + O_3$	2.47 (1.06 to 3.90)	2.77 (−0.82 to 6.48)	−0.26 (−15.60 to 17.86)
Respiratory			
SO_2	1.84 (0.29 to 3.41)	2.84 (−0.99 to 6.82)	12.75 (−2.59 to 30.51)
$SO_2 + PM_{10}$	1.24 (−0.39 to 2.90)	2.24 (−1.60 to 6.23)	12.98 (−2.35 to 30.71)
$SO_2 + NO_2$	0.23 (−1.68 to 2.17)	1.08 (−2.88 to 5.19)	11.57 (−3.71 to 29.27)
$SO_2 + O_3$	1.77 (0.11 to 3.46)	2.58 (−1.40 to 6.73)	14.49 (−7.53 to 41.75)
Cardiopulmonary			
SO_2	1.28 (0.56 to 2.01)	1.43 (−0.46 to 3.36)	2.26 (−4.05 to 8.98)
$SO_2 + PM_{10}$	0.93 (0.17 to 1.70)	1.11 (−0.79 to 3.04)	1.92 (−4.36 to 8.62)
$SO_2 + NO_2$	0.38 (−0.51 to 1.28)	0.49 (−1.46 to 2.48)	1.57 (−4.70 to 8.25)
$SO_2 + O_3$	1.19 (0.41 to 1.98)	1.73 (−0.24 to 3.75)	0.70 (−7.95 to 10.17)
Non-cardiopulmonary			
SO_2	0.87 (0.13 to 1.62)	1.66 (−0.46 to 3.81)	2.39 (−3.63 to 8.77)
$SO_2 + PM_{10}$	0.68 (−0.11 to 1.47)	1.43 (−0.70 to 3.61)	2.00 (−3.99 to 8.36)
$SO_2 + NO_2$	0.14 (−0.77 to 1.06)	0.82 (−1.36 to 3.04)	1.90 (−4.09 to 8.26)
$SO_2 + O_3$	0.91 (0.13 to 1.71)	1.87 (−0.38 to 4.17)	−2.11 (−10.19 to 6.70)

[a] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

[b] Estimates were obtained from the main effect and pollutant × temperature interaction models. The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothing functions for time, daily mean temperature, and daily mean RH; local smoothing over 2 peaks of mortality and the remaining period; and indicators for season.

[c] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table E.6. Copollutant Regression Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in O_3 Concentration by Temperature, for Lag 0–1 Day, July 1, 2000, to June 30, 2004[a,b]

	Temperature		
	Normal	Low	High
Cause of Death[c] / Pollutant(s)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural			
O_3	0.19 (−0.15 to 0.54)	0.68 (−0.83 to 2.21)	1.41 (0.23 to 2.61)
$O_3 + PM_{10}$	0.16 (−0.18 to 0.50)	0.52 (−0.98 to 2.04)	1.20 (0.02 to 2.39)
$O_3 + NO_2$	0.02 (−0.33 to 0.36)	0.33 (−1.16 to 1.85)	1.10 (−0.07 to 2.29)
$O_3 + SO_2$	0.06 (−0.29 to 0.41)	0.38 (−1.12 to 1.90)	1.25 (0.07 to 2.44)
Cardiovascular			
O_3	−0.25 (−0.72 to 0.22)	0.09 (−1.94 to 2.15)	1.39 (−0.25 to 3.06)
$O_3 + PM_{10}$	−0.25 (−0.71 to 0.22)	0.00 (−2.01 to 2.06)	1.16 (−0.47 to 2.82)
$O_3 + NO_2$	−0.39 (−0.86 to 0.08)	−0.20 (−2.22 to 1.85)	1.09 (−0.54 to 2.74)
$O_3 + SO_2$	−0.37 (−0.84 to 0.10)	−0.21 (−2.23 to 1.85)	1.22 (−0.41 to 2.88)
Stroke			
O_3	−0.27 (−0.81 to 0.28)	0.57 (−1.91 to 3.10)	1.09 (−0.77 to 2.98)
$O_3 + PM_{10}$	−0.28 (−0.82 to 0.26)	0.48 (−1.99 to 3.01)	0.87 (−0.98 to 2.76)
$O_3 + NO_2$	−0.42 (−0.97 to 0.13)	0.27 (−2.19 to 2.80)	0.78 (−1.07 to 2.66)
$O_3 + SO_2$	−0.37 (−0.92 to 0.18)	0.37 (−2.11 to 2.90)	0.96 (−0.89 to 2.85)
Cardiac			
O_3	−0.64 (−1.44 to 0.16)	−0.04 (−3.39 to 3.42)	1.45 (−1.47 to 4.46)
$O_3 + PM_{10}$	−0.61 (−1.41 to 0.19)	−0.17 (−3.51 to 3.28)	1.26 (−1.66 to 4.27)
$O_3 + NO_2$	−0.77 (−1.57 to 0.04)	−0.40 (−3.74 to 3.06)	1.16 (−1.76 to 4.16)
$O_3 + SO_2$	−0.82 (−1.62 to −0.01)	−0.58 (−3.91 to 2.86)	1.20 (−1.71 to 4.19)
Respiratory			
O_3	−0.06 (−1.09 to 0.99)	1.14 (−2.88 to 5.33)	2.98 (−0.79 to 6.90)
$O_3 + PM_{10}$	−0.06 (−1.09 to 0.98)	0.84 (−3.16 to 5.02)	2.57 (−1.19 to 6.48)
$O_3 + NO_2$	−0.37 (−1.41 to 0.67)	0.53 (−3.48 to 4.71)	2.41 (−1.34 to 6.31)
$O_3 + SO_2$	−0.27 (−1.31 to 0.79)	0.65 (−3.37 to 4.83)	2.72 (−1.04 to 6.63)
Cardiopulmonary			
O_3	0.04 (−0.42 to 0.50)	−0.01 (−1.89 to 1.92)	1.51 (−0.11 to 3.16)
$O_3 + PM_{10}$	−0.01 (−0.46 to 0.45)	−0.22 (−2.10 to 1.69)	1.37 (−0.24 to 3.00)
$O_3 + NO_2$	−0.18 (−0.63 to 0.29)	−0.45 (−2.32 to 1.46)	1.26 (−0.34 to 2.89)
$O_3 + SO_2$	−0.13 (−0.60 to 0.34)	−0.38 (−2.26 to 1.54)	1.45 (−0.16 to 3.08)
Non-cardiopulmonary			
O_3	0.22 (−0.22 to 0.66)	1.39 (−0.74 to 3.57)	0.50 (−1.01 to 2.02)
$O_3 + PM_{10}$	0.21 (−0.23 to 0.65)	1.26 (−0.87 to 3.42)	0.37 (−1.13 to 1.90)
$O_3 + NO_2$	0.09 (−0.35 to 0.54)	1.10 (−1.03 to 3.26)	0.30 (−1.20 to 1.82)
$O_3 + SO_2$	0.14 (−0.31 to 0.58)	1.12 (−1.01 to 3.29)	0.41 (−1.10 to 1.94)

[a] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

[b] Estimates were obtained from the main effect and pollutant × temperature interaction models. The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothing functions for time, daily mean temperature, and daily mean RH; local smoothing over 2 peaks of mortality and the remaining period; and indicators for season.

[c] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table E.7. Mean Percentage Change in Daily Cause-Specific Mortality, Evaluated at Lag 0–1 Day, Using the Simple Averaging and Centering Approaches, July 1, 2000, to June 30, 2004[a,b]

Cause of Death[c] / Statistical Approach	PM_{10} Mean % Change (95% CI)	NO_2 Mean % Change (95% CI)	SO_2 Mean % Change (95% CI)
All natural			
Averaging	0.43 (0.24 to 0.62)	1.96 (1.30 to 2.62)	1.20 (0.66 to 1.74)
Centering	0.42 (0.23 to 0.61)	1.92 (1.26 to 2.59)	1.19 (0.65 to 1.74)
Cardiovascular			
Averaging	0.57 (0.31 to 0.84)	2.12 (1.18 to 3.06)	1.47 (0.70 to 2.25)
Centering	0.57 (0.31 to 0.84)	2.13 (1.19 to 3.07)	1.47 (0.70 to 2.26)
Stroke			
Averaging	0.57 (0.25 to 0.88)	2.17 (1.07 to 3.28)	1.10 (0.19 to 2.02)
Centering	0.56 (0.25 to 0.87)	2.20 (1.09 to 3.31)	1.10 (0.19 to 2.02)
Cardiac			
Averaging	0.49 (0.04 to 0.94)	2.02 (0.44 to 3.62)	2.04 (0.74 to 3.37)
Centering	0.49 (0.04 to 0.94)	1.93 (0.35 to 3.54)	2.02 (0.71 to 3.35)
Respiratory			
Averaging	0.87 (0.34 to 1.41)	3.69 (1.78 to 5.64)	2.10 (0.58 to 3.63)
Centering	0.86 (0.32 to 1.40)	3.60 (1.68 to 5.55)	2.06 (0.54 to 3.60)
Cardiopulmonary			
Averaging	0.52 (0.27 to 0.77)	2.17 (1.29 to 3.05)	1.33 (0.62 to 2.05)
Centering	0.51 (0.26 to 0.77)	2.14 (1.26 to 3.02)	1.32 (0.61 to 2.04)
Non-cardiopulmonary			
Averaging	0.30 (0.05 to 0.54)	1.66 (0.79 to 2.53)	1.01 (0.29 to 1.73)
Centering	0.30 (0.05 to 0.54)	1.61 (0.74 to 2.49)	1.01 (0.29 to 1.73)

[a] O_3 is not included because only one monitor was used in reporting O_3 concentrations.

[b] The covariates considered in the GAM are indicators of days of the week; 2 peaks of mortality; extreme cold weather; extreme hot weather; extreme humid weather; smoothing functions for time, daily mean temperature, and daily mean RH; and local smoothing over 2 peaks of mortality and the remaining period.

[c] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

Table E.8. Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in Concentration of Pollutant, for Lag 0–1 Day, July 1, 2000, to June 30, 2004, Excluding Data for the Peak Mortality Periods[a]

	PM_{10}	NO_2	SO_2	O_3
Cause of Death[b]	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural	0.46 (0.28 to 0.65)	2.14 (1.50 to 2.78)	1.25 (0.71 to 1.80)	0.16 (−0.18 to 0.50)
Cardiovascular	0.54 (0.27 to 0.81)	2.00 (1.07 to 2.94)	1.54 (0.76 to 2.31)	−0.19 (−0.65 to 0.27)
Stroke	0.53 (0.21 to 0.84)	1.95 (0.86 to 3.06)	1.14 (0.23 to 2.05)	−0.20 (−0.73 to 0.34)
Cardiac	0.48 (0.02 to 0.94)	2.14 (0.56 to 3.75)	2.26 (0.94 to 3.59)	−0.55 (−1.33 to 0.24)
Respiratory	1.07 (0.59 to 1.55)	4.53 (2.84 to 6.25)	2.04 (0.64 to 3.45)	−0.07 (−0.99 to 0.85)
Cardiopulmonary	0.57 (0.33 to 0.81)	2.34 (1.51 to 3.18)	1.37 (0.67 to 2.07)	0.06 (−0.38 to 0.51)
Non-cardiopulmonary	0.34 (0.09 to 0.59)	1.76 (0.88 to 2.66)	1.02 (0.27 to 1.76)	0.23 (−0.20 to 0.67)

[a] The covariates considered in the GAM are indicators of days of the week; extreme cold weather; extreme hot weather; extreme humid weather; and smoothing functions for time, daily mean temperature, and daily mean RH, excluding data for July 28, 2003–August 08, 2003, and December 1, 2003–December 31, 2003.

[b] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

APPENDIX F. Exposure–Response Curves for O_3

Table F.1. Generalized Cross-Validation Statistics for Various Regression Models for O_3, for Lag 0–1 Day[a]

	Regression Model								
Cause of Death[b]	Smoothed	Linear	PW25	PW50	PW75	PW100	PW125	PW150	*P* Value[c]
All natural	1.433358	1.433196	1.433708	1.433320	1.434508	1.435317	1.435162	1.433649	0.059
Cardiovascular	1.326422	1.324724	1.326145	1.323902	1.325029	1.325082	1.326391	1.326739	0.357
Stroke	1.136889	1.133756	1.135494	1.135266	1.135543	1.135499	1.135413	1.135478	0.852
Cardiac	1.140715	1.144915	1.143237	1.139253	1.140700	1.142135	1.145807	1.146615	0.016
Respiratory	1.412759	1.406483	1.410376	1.410180	1.410106	1.409328	1.407979	1.406806	0.516
Cardiopulmonary	1.425831	1.423418	1.424387	1.423896	1.425159	1.425443	1.425561	1.425293	0.252
Non-cardiopulmonary	1.067142	1.066064	1.067001	1.067567	1.067692	1.067304	1.067151	1.065435	0.198

[a] The models included the base model plus different specifications of O_3 relationship to the logarithm of cause-specific mortality (i.e., log(death) = base model + f(O_3)). The "smoothed" model specified a smooth function for O_3 (df = 3), and the "linear" model specified a linear function for O_3. The piecewise regression (PW) model allowed the slope of O_3 to change after the cutoff point x (x = 25, 50, 75, 100, 125, and 150, respectively). The model yielding the smallest GCV value indicates the best fit.

[b] ICD-9 codes were applied before January 1, 2003, and ICD-10 codes were applied after December 31, 2002. All natural: ICD-9 1–799 or ICD-10 A00–R99; CVD: ICD-9 390–459 or ICD-10 I00–I99; cerebrovascular disease, or stroke: ICD-9 430–438 or ICD-10 I60–I69; CARD: ICD-9 390–398, 410–429, or ICD-10 I00–I09, I20–I52; RD: ICD-9 460–519 or ICD-10 J00–J98; and cardiopulmonary (RD + CVD): ICD-9 390–459, 460–519, or ICD-10 I00–I99, J00–J98.

[c] *P* value for testing whether the "smoothed" model significantly improved model fit from the "linear" model using the likelihood ratio test (df = 2).

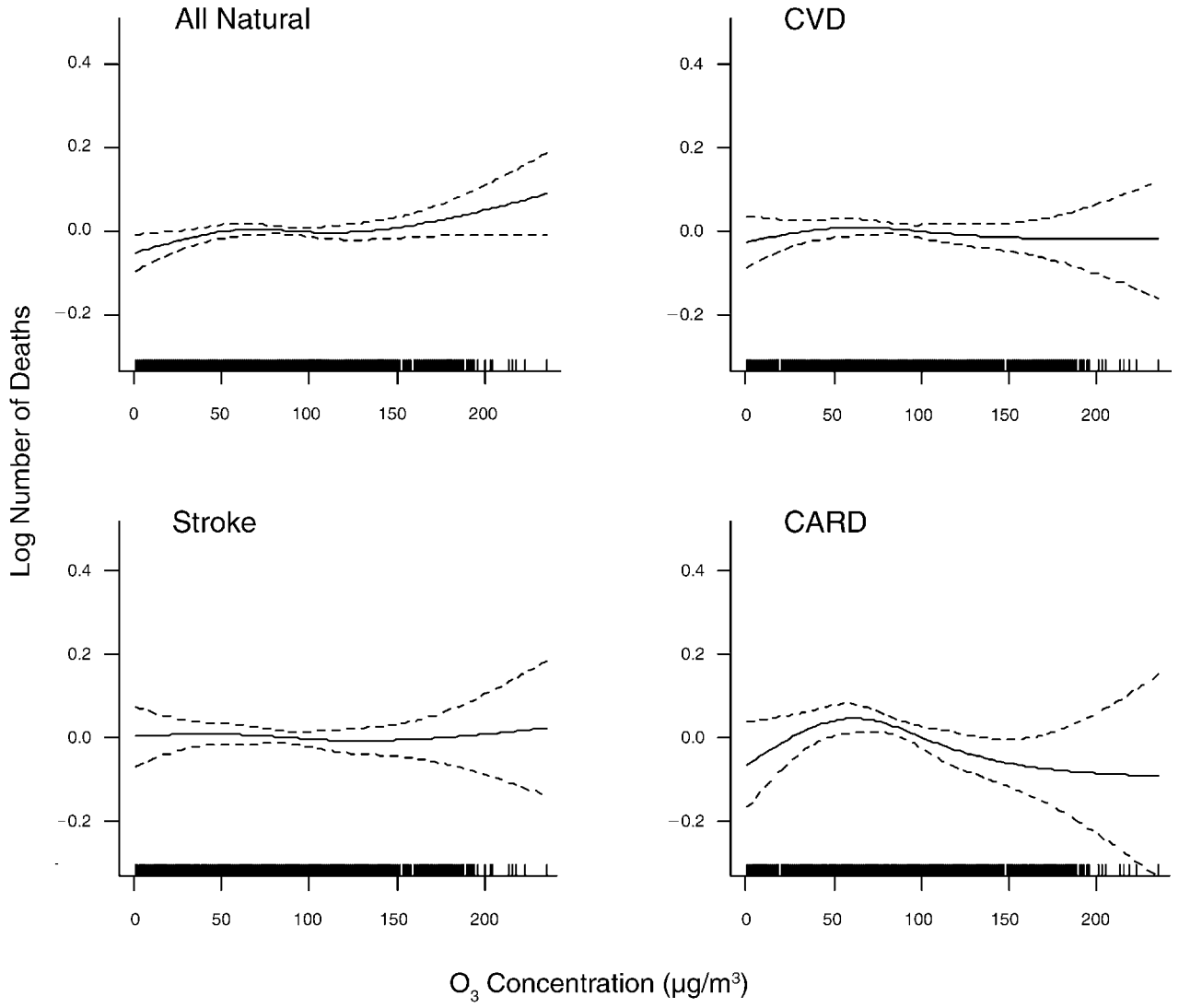

Figure F.1. Exposure–response curves for the mean percentage of change in daily mortality by cause of death evaluated at lag 0–1 day per 10-μg/m^3 increase in O_3 concentration.

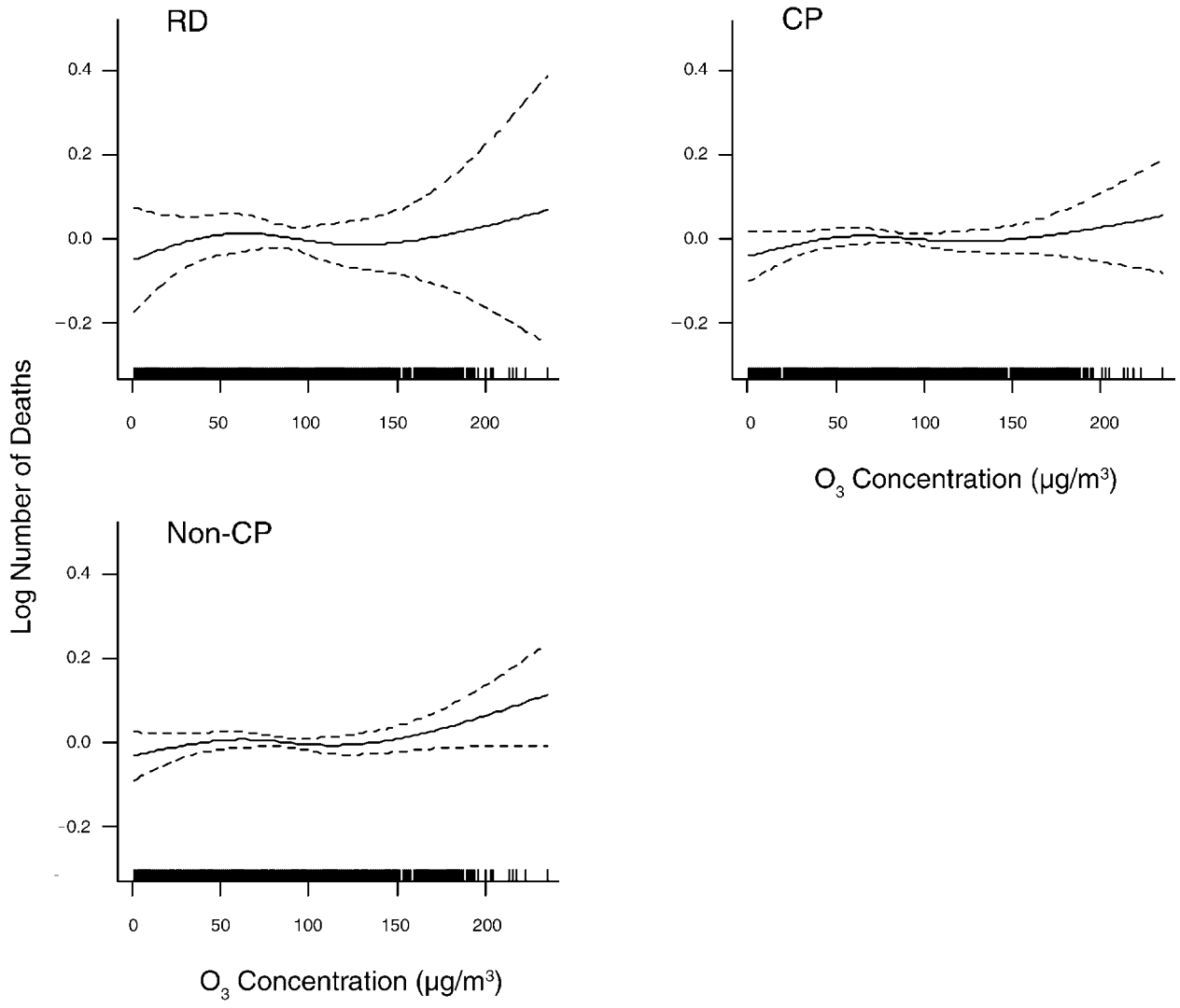

Figure F.1 (*Continued*).

APPENDIX G. Uncertainty of Effect Estimates Due to Change in ICD Coding

MORTALITY DATA

In this study, both ICD-9 and ICD-10 coding was used. To assess the potential uncertainty in the effect estimates introduced by the change from ICD-9-coded mortality data to ICD-10-coded mortality data on January 1, 2003, we added a new research item to this study — the requirement that each district's center for disease control recode 2002 mortality data (originally coded with ICD-9 coding) with ICD-10 coding. We then had both ICD-9- and ICD-10-coded mortality data for the year 2002. Since analyzing data coding is time-consuming, we focused on only one year of mortality data to identify any potential difference in the estimates of the effects of ambient air pollution on mortality due to the shift in ICD coding.

Each of the nine districts' centers for disease control in Wuhan took responsibility for coding the 2002 mortality data with ICD-10 code strictly according to the standardized collection procedure for mortality statistics in Wuhan (see Appendix J available on the HEI Web site). WCDC centrally managed all mortality data coding and required that the ICD-10 coding be done by the trained and certified personnel who previously coded the data using ICD-9 code in each district. The personnel applied the code to the mortality data strictly according to the underlying cause of death in the original death certificates. In addition, several quality control procedures were followed to ensure data accuracy and consistency, including double data entry of underlying causes of death along with audits of the computer output and death certificates for accuracy.

We found high concordance rates and kappa statistics close to a magnitude of 1 between the ICD-9- and ICD-10-coded mortality data for 2002 (Table G.1). Among the cause-specific mortality groups, the agreement rate ranges from 99.36% (in the Hongshan district) to 100% for CP and non-CP mortality. Similarly, the kappa statistics all exceed 0.98. Most of the coding disagreements occurred in the Hongshan district, where there were three disagreements for CVD and stroke mortality, nine for RD mortality, and six for CP and non-CP mortality (see Table G.1). In the Wuchang district, there was one disagreement for stroke and CARD mortality. The Hannan district had one disagreement each for RD, CP, and non-CP mortality. These slight coding disagreements are thought to be caused by human error at the district center for disease control. The Jiangan, Jianhan, Qiaokou, Hanyang, Qingshan, and Dongxihu districts all had a 100% agreement rate for mortality due to all of the cause-specific categories.

AIR POLLUTION DATA

The pollution data for 2002 were considered complete, with few missing values (Table G.2). We required that each monitor provide data for at least 75% of the days in a year; that at least 75% of each day's measurements be available before calculating the PM_{10}, SO_2, and NO_2 24-hour average concentrations; and that at least six hourly concentrations per day be available before calculating the 8-hour average concentrations of O_3. In 2002, the daily mean concentration was 144.3 $\mu g/m^3$ for PM_{10}, 96.4 $\mu g/m^3$ for O_3, 40.0 $\mu g/m^3$ for SO_2, and 52.9 $\mu g/m^3$ for NO_2. These concentrations are comparable to the daily mean concentrations for the four study years (Table 4 in the main text). We found considerable temporal variations in daily mean concentrations during the year 2002. Time-series plots in Figure 5 (in the main text) show that seasonal cycles account for much of the variability. PM_{10}, SO_2, and NO_2 had peaks in the winters. For O_3, as expected, a peak occurred in the summer months. Spatial variations of daily mean concentrations were also observed (Figures D.1–4 in Appendix D). Despite these variations, we observed that PM_{10}, NO_2, and O_3 were highly correlated between any pair of monitoring stations (Table 6 in the main text).

EFFECT ESTIMATES

Table G.3 shows the estimates of the mean percentage of change in daily mortality per 10-$\mu g/m^3$ increase in the concentration of pollutants by cause of death and ICD coding. We found little change in the estimated effects at lag 0–1 day across all cause-specific mortality, as well as across the four studied pollutants. The maximum change in the estimated effect due to the ICD-coding switch was 0.05% for the effect of NO_2 on CARD and RD mortality. All statistically significant levels of the estimated effects remained unchanged.

Table G.1. Daily Death Counts, Concordance Rates, and Kappa Statistics (κ) Between ICD-9- and ICD-10-Coded Mortality Data, by Cause of Death, ICD Coding, and District, 2002[a]

District / ICD Code	Cardiovascular			Stroke			Cardiac			Respiratory			Cardiopulmonary			Non-cardiopulmonary		
	n	Rate	κ	*n*	Rate	κ	*n*	Rate	κ	*n*	Rate	κ	*n*	Rate	κ	*n*	Rate	κ
Total																		
ICD-9	9877	99.99	0.9997	6475	99.98	0.9996	2904	100.0	0.9998	2551	99.95	0.9978	12428	99.94	0.9988	9402	99.94	0.9988
ICD-10	9874			6471			2905			2561			12435			9395		
Jiangan																		
ICD-9	1732	100.0	1.0000	1184	100.0	1.0000	505	100.0	1.0000	551	100.0	1.0000	2283	100.0	1.0000	1624	100.0	1.0000
ICD-10	1732			1184			505			551			2283			1624		
Jianhan																		
ICD-9	1107	100.0	1.0000	684	100.0	1.0000	354	100.0	1.0000	282	100.0	1.0000	1389	100.0	1.0000	1392	100.0	1.0000
ICD-10	1107			684			354			282			1389			1392		
Qiaokou																		
ICD-9	1710	100.0	1.0000	1145	100.0	1.0000	472	100.0	1.0000	385	100.0	1.0000	2095	100.0	1.0000	1425	100.0	1.0000
ICD-10	1710			1145			472			385			2095			1425		
Hanyang																		
ICD-9	1012	100.0	1.0000	711	100.0	1.0000	231	100.0	1.0000	265	100.0	1.0000	1277	100.0	1.0000	973	100.0	1.0000
ICD-10	1012			711			231			265			1277			973		
Wuchang																		
ICD-9	1915	100.0	1.0000	1258	99.97	0.9994	573	99.97	0.9990	415	100.0	1.0000	2330	100.0	1.0000	1592	100.0	1.0000
ICD-10	1915			1257			574			415			2330			1592		
Qingshan																		
ICD-9	864	100.0	1.0000	523	100.0	1.0000	293	100.0	1.0000	216	100.0	1.0000	1080	100.0	1.0000	1041	100.0	1.0000
ICD-10	864			523			293			216			1080			1041		
Hongshan																		
ICD-9	816	99.84	0.9967	496	99.84	0.9959	254	100.0	1.0000	288	99.52	0.9818	1104	99.36	0.9868	775	99.36	0.9868
ICD-10	813			493			254			297			1110			769		
Dongxihu																		
ICD-9	527	100.0	1.0000	362	100.0	1.0000	153	100.0	1.0000	92	100.0	1.0000	619	100.0	1.0000	462	100.0	1.0000
ICD-10	527			362			153			92			619			462		
Hannan																		
ICD-9	194	100.0	1.0000	112	100.0	1.0000	69	100.0	1.0000	57	99.73	0.9897	251	99.73	0.9938	118	99.73	0.9938
ICD-10	194			112			69			58			252			117		

[a] January 1, 2002, to December 31, 2002.

Table G.2. Distributions of Mean Daily Ambient Air Pollutants and Weather Variables, 2002[a]

Pollutant (μg/m^3) / Weather Variable	*n* (Days)	Mean (SD)	Minimum	Maximum	Percentile		
					25th	50th	75th
PM_{10}	365	144.3 (66.2)	33.4	421.8	93.8	133.4	178.8
NO_2	365	52.9 (19.4)	23.8	127.4	38.8	47.2	62.8
SO_2[b]	365	40.0 (27.6)	6.3	187.8	21.0	32.3	51.5
O_3[c]	354	96.4 (48.7)	1.8	258.5	59.5	90.6	126.9
Daily mean temperature (°C)	365	18.1 (8.7)	−2.5	34.7	10.6	18.0	25.5
Daily mean relative humidity (%)	365	75.9 (11.9)	45.0	98.0	67.0	76.0	86.0

[a] January 1, 2002, to December 31, 2002.

[b] Excluding the station 4 (Wugang) monitor.

[c] Only station 5 (Donghu) provided valid measurements of O_3; daily 8-hour concentrations (10:00–18:00) were used.

Table G.3. Estimates of the Mean Percentage Change in Daily Mortality per 10-μg/m^3 Increase in Concentration of Pollutants, for Lag 0-1 Day, by Cause of Death and ICD Coding, 2002

Cause of Death / ICD Code[a]	PM_{10}	NO_2	SO_2	O_3
	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)	Mean % Change (95% CI)
All natural				
ICD-9	0.34 (−0.06 to 0.74)	1.90 (0.56 to 3.24)	0.80 (−0.18 to 1.79)	1.08 (0.41 to 1.76)
ICD-10	0.34 (−0.06 to 0.74)	1.90 (0.56 to 3.24)	0.80 (−0.18 to 1.79)	1.08 (0.41 to 1.76)
Cardiovascular				
ICD-9	0.60 (0.06 to 1.14)	1.48 (−0.42 to 3.41)	0.19 (−1.18 to 1.58)	0.98 (0.03 to 1.94)
ICD-10	0.60 (0.06 to 1.14)	1.49 (−0.41 to 3.42)	0.19 (−1.18 to 1.58)	0.99 (0.03 to 1.95)
Stroke				
ICD-9	0.29 (−0.42 to 0.99)	0.87 (−1.51 to 3.30)	0.30 (−1.39 to 2.03)	1.09 (−0.10 to 2.30)
ICD-10	0.28 (−0.42 to 0.99)	0.87 (−1.50 to 3.29)	0.29 (−1.40 to 2.01)	1.10 (−0.09 to 2.30)
Cardiac				
ICD-9	0.50 (−0.43 to 1.43)	0.65 (−2.49 to 3.90)	0.89 (−1.41 to 3.24)	0.24 (−1.38 to 1.89)
ICD-10	0.51 (−0.42 to 1.44)	0.70 (−2.44 to 3.95)	0.91 (−1.39 to 3.26)	0.26 (−1.36 to 1.91)
Respiratory				
ICD-9	0.96 (0.05 to 1.88)	3.58 (0.41 to 6.85)	0.96 (−1.29 to 3.26)	1.23 (−0.44 to 2.92)
ICD-10	0.92 (0.01 to 1.85)	3.63 (0.45 to 6.91)	0.99 (−1.26 to 3.29)	1.25 (−0.42 to 2.95)
Cardiopulmonary				
ICD-9	0.69 (0.22 to 1.17)	2.28 (0.65 to 3.93)	0.46 (−0.75 to 1.68)	1.02 (0.17 to 1.88)
ICD-10	0.68 (0.21 to 1.16)	2.30 (0.67 to 3.95)	0.47 (−0.74 to 1.69)	1.03 (0.17 to 1.89)
Non-cardiopulmonary				
ICD-9	0.29 (−0.24 to 0.82)	2.81 (1.02 to 4.64)	1.15 (−0.16 to 2.47)	0.99 (0.13 to 1.85)
ICD-10	0.31 (−0.22 to 0.84)	2.79 (1.00 to 4.61)	1.13 (−0.17 to 2.45)	0.97 (0.11 to 1.84)

[a] ICD-9-coded mortality data, January 1, 2002, to December 31, 2002; ICD-10-coded mortality data, January 1, 2002, to December 31, 2002.

APPENDIX H. HEI Quality Assurance Statement

The conduct of this study was subjected to periodic, independent audits by a team from Hoover Consultants. This team consisted of auditors with experience in toxicology, epidemiology, and air quality data. The audits included in-process monitoring of study activities for conformance to the study protocol and examination of records and supporting data. The dates of each audit are listed in the table below with the phase of the study examined:

QUALITY ASSURANCE AUDITS

Date	Phase of Study
May 19–20, 2005	Data for mortality, air quality parameters, and meteorology were audited. Documentation was examined for personnel qualifications and experience. Prior to this audit, the investigators conducted an internal audit and the auditors reviewed that documentation. The audit team visited the Center for Environmental Monitoring in Wuhan, China, and had an opportunity to visit the Donghu and Jiangan air monitoring sites (two of the six sites) used in this study. Raw data from individual monitors were electronically relayed to the Center for Environmental Monitoring, where a validation procedure was performed prior to archiving along with original maintenance and calibration records. The audit compared daily values from the Center's printed archival data records to a hard copy of the electronic study file, examining 6 days in 2000, 9 days at Hanyang in 2001, 12 days at Jiangan in 2002, 16 days at Wugang in 2003, 12 days at Nanzhan in 2003, and 6 days at Jiangtan in 2004. Periods of missing data were traced back to maintenance records to verify that documentation existed. One apparent discrepancy was noted for NO_2 at Nanzhan on 12/23/03, where the archival printout recorded 127 micrograms per cubic meter and the entry in Zhengmin Qian's electronic study file was 131. This difference was resolved by Dr. Qian's explanation that his calculations included a few raw hourly values that had been excluded by the Center from the archival record. Hourly data in the electronic study file were verified against archival records for all pollutants on each May 1 in the study, a date chosen because PM concentrations were often observed to spike during the Labor Day holiday due to fireworks usage. Calculated daily minima and maxima were also verified from the archival hourly records for an additional five days. At the Centres for Disease Prevention and Control, also in Wuhan, the audit team followed the extraction of data from the second copy of 50 of the original death certificates through to the electronic files. Variables checked on each of these death certificates included a multi-digit resident registration number, gender, date of birth, date of death, and ICD-9 or ICD-10 code for underlying cause of death. For 16 death certificates, the auditors verified that the Chinese description for the underlying cause of death matched the respective ICD code. The audit consisted of retracing the data from the original sources of development to the secondary electronic data sets received by the investigators through to the analysis file generated at Pennsylvania State University. The audit team used the 10-Month Progress Report as the basis for auditing the data in this study. Statements in the text of the report were compared to the subsequent tables, figures, and data files. The report was reviewed for internal consistency. This study is being conducted in accordance with two protocols: one for the site-specific aspects of the study that apply to Wuhan and the Common Protocol for the HEI time series. The audit team reviewed both of these documents to determine that the study was being conducted in conformance with these requirements.
June 20, 2005	Secondary files of death certificate data, previously audited in Wuhan, were audited against the final analysis file for the 50 death certificates in the audit sample.
April 6, 2008	A draft of the final study report was examined for internal consistency

and conformance with the study proposal. Comments were provided to HEI via e-mail.

A written report of the first two inspections was provided to the Director of Science of the Health Effects Institute who transmitted these findings to the Principal Investigator. These quality assurance audits demonstrated that the study was conducted by experienced professionals in accordance with the original study proposal. The report appears to be an accurate representation of the study.

B. Kristin Hoover
Hoover Consultants

APPENDICES AVAILABLE ON THE WEB

The following materials may be obtained from HEI's Web site, *www.healtheffects.org*:

Appendix I. Standard Operating Procedure for Ambient Air Pollution Data Collection in Wuhan

Appendix J. Standard Operating Procedure for Mortality Data Collection in Wuhan

ABOUT THE AUTHORS

Zhengmin Qian, M.D., Ph.D., is an associate professor of epidemiology at Saint Louis University in St. Louis, Missouri, U.S.A. He was an assistant professor from 2002 to 2008 at the Pennsylvania State University College of Medicine in Hershey, Pennsylvania, U.S.A., and Investigator II and codirector from 2008 to 2010 at the Environmental Health Institute, Geisinger Center for Health Research, Danville, Pennsylvania. From 1987 to 2001 he was a key investigator on the study "Health Effects of Long-term Air Pollution on Lung Function and Respiratory Health in Children and Adults in Four Chinese Cities" sponsored by the U.S. Environmental Protection Agency under Annex 1 of the China–U.S. Protocol for Scientific and Technical Cooperation in the Field of Environment Protection. His research interests include exposure assessment and the health effects of environmental and occupational exposure.

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OTHER PUBLICATIONS RESULTING FROM THIS RESEARCH

Health Effects Institute. 2008. Public Health and Air Pollution in Asia (PAPA): Key Results from Bangkok, Hong Kong, Shanghai, and Wuhan. Communication 13. Health Effects Institute, Boston, MA.

Qian Z, He Q, Lin HM, Kong L, Bentley CM, Liu W, Zhou D. 2008. High temperatures enhanced acute mortality effects of ambient particle pollution in the "oven" city of Wuhan, China. Environ Health Perspect 116(9):1172–1178.

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ABBREVIATIONS AND OTHER TERMS

APHEA	Air Pollution and Health: A European Approach
APHENA	Air Pollution and Health: A European and North American Approach
CARD	cardiac or heart disease
CI	confidence interval
CVD	cardiovascular disease
CP	cardiopulmonary disease
df	degrees of freedom
GAM	generalized additive model
GCV	generalized cross-validation
HES	Health Evaluation Sciences department
ICD-9	*International Classification of Diseases*, 9th revision
ICD-10	*International Classification of Diseases*, 10th revision
ISOC	International Scientific Oversight Committee (HEI)
NMMAPS	National Mortality, Morbidity and Air Pollution Studies
NO_2	nitrogen dioxide
O_3	ozone
PAPA	Public Health and Air Pollution in Asia
PACF	partial autocorrelation function
PM	particulate matter
PM_{10}	particulate matter $\leq$ 10 μm in aerodynamic diameter
$PM_{10-2.5}$	particulate matter $\leq$ 10 μm and $\geq$ 2.5 μm in aerodynamic diameter
RD	respiratory disease
RH	relative humidity
SO_2	sulfur dioxide
SOP	Standard Operating Procedure
U.S. EPA	U.S. Environmental Protection Agency
WAAMS	Wuhan Air Automatic Monitoring System
WAES	Wuhan Academy of Environmental Science
WCDC	Wuhan Centres for Disease Prevention and Control
WEMC	Wuhan Environmental Monitoring Center
WMA	Wuhan Meteorological Administration

Research Report 154, Part 2. *Association of Daily Mortality with Ambient Air Pollution, and Effect Modification by Extremely High Temperature in Wuhan, China*, Z. Qian et al.

INTRODUCTION

The study by Zhengmin Qian from the Pennsylvania State University College of Medicine and colleagues, titled Association of Daily Mortality with Ambient Air Pollution, and Effect Modification by Extremely High Temperature in Wuhan, China, was conducted as part of a coordinated suite of time-series studies of the health effects of short-term exposure to air pollution in major Asian cities, a major component of HEI's Public Health and Air Pollution in Asia (PAPA*) program. Information on the origins, objectives, and scope of the PAPA program are provided in the Preface to this volume. Background information on the health and environmental conditions in Wuhan, China, are available in the Overview for all five PAPA studies, also at the beginning of this volume.

Previous studies of air pollution effects on morbidity in several Chinese cities had established that the annual average concentration of total suspended particulate matter (PM) in Wuhan exceeded the Chinese mean annual standard of 200 μg/m^3 (Qian et al. 2001; Zhang et al. 2002) and that the average PM_{10} levels in Wuhan are much greater than the levels recorded in the United States (He et al. 1993). The levels of air pollutants measured in Wuhan had also been associated with respiratory morbidity in children in a cross-sectional study of four Chinese cities (Zhang et al. 2002). Wuhan has also been called an "oven city," because of the lengthy periods of extreme heat during a typical summer. The wide range of daily pollutant concentrations, including occasionally high pollutant concentrations, and the extreme summer heat provide an unusual opportunity to study how heat and pollution levels may combine to affect mortality.

SPECIFIC AIMS

The team proposed to determine whether daily mean variations in ambient PM_{10} concentrations during the years 2000 to 2004 in Wuhan, China, were associated with daily variations in all natural (nonaccidental, all-cause) mortality and with daily cause-specific mortality. Additional analyses were aimed at elucidating the relationships between extreme heat, air pollution, and mortality, and at assessing possible biases when mortality coding schemes were changed.

The specific aims addressed were as follows:

1. To examine associations of daily mortality due to all natural causes and daily cause-specific mortality with daily mean concentrations of PM ≤ 10 μm in aerodynamic diameter (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone (O_3) in line with the Common Protocol used by all 5 PAPA studies (found at the end of this volume).
2. To determine interactions between air pollution and extremely high temperature on daily mortality due to all natural causes and daily cause-specific mortality.
3. To assess the uncertainty of effect estimates caused by the change in the *International Classification of Diseases* (ICD) coding of mortality data from revision 9 (ICD-9) to revision 10 (ICD-10) code during the study period.

DATA SOURCES

MORTALITY DATA

Computerized daily mortality data were obtained for the study period through the Wuhan Centres for Disease Prevention and Control. The cause of death was coded by ICD-9 and ICD-10 classifications from July 1, 2000, to December 31, 2002, and from January 1, 2003, to June 30, 2004, respectively. Deaths were stratified into accidental and nonaccidental, with nonaccidental deaths further

Dr. Zhengmin Qian's 2-year study "Ambient particle air pollution and daily mortality in Wuhan" began in July 2004. Total expenditures were $150,063. The draft Investigators' Report from Qian and colleagues was received for review in August 2006. The revised report received in October 2007, was accepted for publication in December 2007. During the review process, the HEI Health Review Committee and the investigators had the opportunity to exchange comments and to clarify issues in both the Investigators' Report and the Review Committee's Commentary.

* A list of abbreviations and other terms appears at the end of the Investigators' Report.

stratified into the following categories: all natural, cardiovascular, cerebrovascular, cardiac, respiratory, cardiopulmonary, and total non-cardiopulmonary.

AIR POLLUTANT DATA

Air pollutant data were collected from air quality monitors operated by the Wuhan Environmental Monitoring Center as part of the Wuhan Air Automatic Monitoring System. Those monitors follow quality assurance and control procedures set by the State Environmental Protection Administration of China, and provide continuous data. Specific species' indicators (e.g., 8-hour mean O_3) used in this study are derived from those measurements. The PM_{10} and NO_2 concentrations were collected from five ambient monitoring stations, and the SO_2 concentrations from four, though ambient O_3 concentrations from only one monitor were used. SO_2 data from one monitor near a smelter facility were not used, as the researchers determined that the extreme levels of SO_2 measured at this station were not representative of citywide exposures; however, they did use data from this station for other pollutants. Daily data that met the criteria and were deemed acceptable were averaged using centering to obtain the value for use in the air quality–health association analyses (see the Discussion in the Investigators' Report). While there were sufficient data to calculate the average values for SO_2, NO_2, and PM_{10} concentrations for almost the entire period, O_3 values were missing for 75 of the 1461 days.

METEOROLOGIC DATA

Meteorologic data for daily average temperature and humidity were obtained from the Wuhan Meteorological Administration.

DATA ANALYSIS

Main statistical analyses were conducted in line with the Common Protocol for the PAPA program using generalized additive models to examine associations between daily mortality (total nonaccidental and cause-specific) and air pollution. Regression models were used with natural spline smoothers with 3 to 8 degrees of freedom (df) per year to control for time trend and 3 df to control for potential confounding effects of meteorology. Exact degrees of freedom for the time-trend spline were selected from within the 3 to 8 df per year range by reference to the properties of the residuals of the competing models. Additionally, special additional time spline terms were included to allow for two periods of anomalously high mortality. Two-day moving averages of current and previous-day concentrations of pollutants (lag 0–1 day) were used in the main analyses, which included a term for the current day's temperature (lag 0 day). Unless otherwise specified, all results are presented as the percent change in daily mortality per 10-$\mu g/m^3$ increase in the two-day moving average of the respective pollutants.

In sensitivity analyses, the impacts of alternative specifications of pollutant lag structures, extended temperature lags, different degrees of temporal smoothing, the inclusion of copollutants, the change in ICD coding, and a term for influenza epidemic were examined. Subgroup analyses by age and sex were also explored to assess subgroup susceptibility. All analyses were conducted in R software, using the mgcv package.

Beyond the Common Protocol and sensitivity analyses just described, the investigators conducted additional analyses to investigate the potential modification of air pollutant effects on daily mortality by extreme temperatures in Wuhan. For these analyses, three weather indicators were created for temperature to denote extremely cold, normal, and hot weather conditions. Extreme temperatures were defined as occurring on days whose average temperatures were above or below the 95th and 5th percentiles of the 4 years of data. Using interaction models, associations of pollutants with mortality were then estimated separately for extreme low, extreme high, and "normal" temperatures. In these models the lag 0 day temperature spline was also retained.

RESULTS

Commentary Tables 1 through 3 and the following paragraphs summarize the key findings from the Qian Investigators' Report.

DAILY MORTALITY AND POLLUTANT INFORMATION

Commentary Table 1, which summarizes information from Qian Investigators' Report Table 7 and Table C.11, shows that during the study period (2000–2004) Wuhan had an average of 61 deaths per day from all natural

Commentary Table 1. Average Daily Mortality in Wuhan During Study Period for Total All Natural Mortality and Selected Other Categories of Cause of Death

Cause of Death	Deaths per Day (Variance)
All natural	61.0 (248.9)
Cardiovascular	27.8 (77.9)
Cardiovascular ≥ age 65	22.4 (59.7)
Respiratory	7.0 (33.4)

Commentary Table 2. Mean 24-Hour Air Pollutant Concentrations, Temperature, and Relative Humidity in Wuhan During Study Period, with Data for Low Temperature Days and High Temperature Days[a]

Pollutant (μg/m^3) / Weather Variable	Mean (SD)	Maximum	Temperature	
			Low Mean (SD)	High Mean (SD)
PM_{10}	141.8 (63.7)	477.8	117.3 (49.5)	96.3 (27.9)
NO_2	51.8 (18.8)	127.4	51.2 (17.8)	32.5 (6.2)
SO_2	39.2 (25.3)	187.8	50.3 (26.7)	23.8 (10.2)
O_3	85.7 (47.0)	258.5	51.5 (24.5)	91.9 (41.8)
Temperature (°C)	17.9 (9.2)	35.8	2.2 (1.3)	33.1 (0.9)
Relative humidity (%)	74.0 (12.5)	99.0	75.3 (16.0)	64.7 (5.6)

[a] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

causes; of these an average of 7.0 deaths per day were classified as respiratory and 27.8 as cardiovascular.

Commentary Table 2 shows the mean and maximum 24-hour concentrations of PM_{10}, SO_2, NO_2, and O_3 and mean and maximum temperature and relative humidity during the study period. The table shows very elevated levels of PM_{10} and SO_2 in Wuhan, though O_3 levels were moderate for a warm and sunny climate. Day-to-day variability in pollutant levels was large during the study (see Table 4 of the Investigators' Report).

In addition, the investigators reported moderate correlations between PM_{10} and NO_2 (partial correlation, $r = 0.59$) and NO_2 and SO_2 ($r = 0.57$). PM_{10} and O_3 were weakly correlated ($r = 0.09$), as were O_3 and NO_2 ($r = 0.20$) (see Qian Investigators' Report Table 6).

ASSOCIATIONS BETWEEN DAILY MORTALITY AND INDIVIDUAL POLLUTANTS

Commentary Table 3 (summarizing Qian Investigators' Report Tables 19 and E.1) shows the key associations between individual pollutants and daily deaths by cause of mortality in single-pollutant models.

MAIN FINDINGS

Using the mean pollutant concentration at lag 0–1 day, short-term increases in the concentrations of PM_{10}, NO_2, and SO_2 (but not O_3) were significantly associated with increased daily all natural mortality (Qian Investigators' Report Tables 8 and 12). Effects estimates (excess risk) were generally larger in people 65 or older, particularly for those who died of cardiovascular causes (Qian Investigators' Report Tables 9 and 13). The effect estimate for the category of respiratory deaths was higher than that of other categories of death (Qian Investigators' Report Tables 9 and 13). PM_{10}, NO_2, and SO_2 were also statistically significantly associated with increases in nonaccidental, noncardiopulmonary mortality. Effect estimates for this stratum of deaths were typically not larger in the subgroup age 65 or older, except for SO_2 (Qian Investigators' Report Tables 9 and 13). No findings on the stratum of accidental deaths were reported.

SENSITIVITY TESTING

The positive associations between individual pollutants and daily mortality in single-pollutant models were largely robust to differences in model specifications due to degree of smoothing for time or to choice of regression spline (natural or penalized) (see Qian Investigators' Report Figures 8 and 9 for PM_{10}; 11 and 13 for NO_2; 12 and 14 for SO_2; and E.1 and E.2 for O_3). The effects of PM_{10} were only slightly attenuated by the inclusion of longer lags for humidity and temperature (Investigators' Report Tables 8 and E.1), but effects of NO_2 and SO_2 (Investigators' Report Table E.1) were greatly attenuated, often no longer showing any effect. The effects of PM_{10}, and to a lesser extent NO_2 on several causes of mortality, were larger on days in the upper 5th percentile of temperature (Qian Investigators' Report Table 19).

In two-pollutant models, the associations of PM_{10} (Qian Investigators' Report Table 10) and SO_2 (Qian Investigators' Report Table 15) with total all natural and cardiovascular mortality were greatly attenuated when NO_2 was included in the models. The estimated effects of NO_2 were somewhat attenuated with the inclusion of PM_{10} and also the addition of SO_2 in the models (Qian Investigators' Report Table 14).

Associations between levels of pollutants and mortality outcomes were not sensitive to the changes in coding of

Commentary Table 3. Associations Between Air Pollutants and Daily Mortality in Wuhan, Including Results Within Various Temperature Strata[a]

Temperature[b] / Cause of Death	PM_{10} ER (95% CI)	NO_2 ER (95% CI)	SO_2 ER (95% CI)	O_3 ER (95% CI)
Entire sample				
All natural	0.43 (0.24 to 0.62)	1.96 (1.30 to 2.62)	1.20 (0.66 to 1.74)	0.29 (−0.05 to 0.63)
Cardiovascular	0.57 (0.31 to 0.84)	2.12 (1.18 to 3.06)	1.47 (0.70 to 2.25)	−0.07 (−0.53 to 0.39)
Respiratory	0.87 (0.34 to 1.41)	3.69 (1.78 to 5.64)	2.10 (0.58 to 3.63)	0.12 (−0.89 to 1.15)
Normal				
All natural	0.36 (0.17 to 0.56)	1.89 (1.22 to 2.57)	1.10 (0.55 to 1.66)	0.19 (−0.15 to 0.54)
Cardiovascular	0.39 (0.11 to 0.66)	1.89 (0.95 to 2.84)	1.36 (0.57 to 2.15)	−0.25 (−0.72 to 0.22)
Respiratory	0.80 (0.25 to 1.35)	3.64 (1.69 to 5.63)	1.84 (0.29 to 3.41)	−0.06 (−1.09 to 0.99)
Low				
All natural	0.62 (−0.09 to 1.34)	2.22 (0.16 to 4.32)	1.74 (0.25 to 3.26)	0.68 (−0.83 to 2.21)
Cardiovascular	0.72 (−0.25 to 1.70)	2.03 (−0.78 to 4.92)	1.81 (−0.24 to 3.91)	0.09 (−1.94 to 2.15)
Respiratory	1.07 (−0.76 to 2.95)	3.17 (−2.13 to 8.75)	2.84 (−0.99 to 6.82)	1.14 (−2.88 to 5.33)
High				
All natural	2.20 (0.74 to 3.68)	4.59 (−1.78 to 11.36)	2.56 (−2.11 to 7.45)	1.41 (0.23 to 2.61)
Cardiovascular	3.28 (1.24 to 5.37)	5.23 (−3.71 to 15.00)	0.35 (−6.18 to 7.32)	1.39 (−0.25 to 3.06)
Respiratory	1.15 (−3.54 to 6.07)	7.68 (−12.36 to 32.30)	12.75 (−2.59 to 30.51)	2.98 (−0.79 to 6.90)

[a] All results shown provide associations between pollutants and mortality for the all age groups and both sexes combined.

[b] Normal temperature = between 5th and 95th percentile of daily average temperatures during the 4-year study period; low temperature < 5th percentile; and high temperature > 95th percentile.

causes of death resulting from the transition from ICD-9 to ICD-10 code (Qian Investigators' Report Table G.3).

HEI EVALUATION OF STUDY

The HEI Review Committee assessed the quality of the data, the analytic design and methods, and the results reported by Dr. Qian and colleagues. The Committee then reviewed the investigators' conclusions regarding the effects of short-term exposure to air pollution on mortality and the extent to which these effects were modified by extremes of temperature experienced in Wuhan. General comments on analytical methods in the Common Protocol (found at the end of this volume) that apply to the Wuhan study and other PAPA studies are included in the Integrated Discussion (found in Part 5 of this volume).

ASSESSMENT OF HEALTH OUTCOMES

The systems for the reporting and coding of deaths in Wuhan appear to have been of high quality for the duration of the study period. Dr. Qian's team went to some effort to assess the effect of a transition from the ICD-9 coding of cause of death to the ICD-10 system during the study period, demonstrating that the changeover had little apparent effect on the effect estimates for relationships between pollutant levels and various causes of death. The authors do acknowledge that the accuracy of the coding may vary with the cause of death because of the ambiguity in the disease processes and common comorbid conditions. This is a well-known potential bias in mortality studies. The Committee noted in its review of this report that there were unusual spikes in the death rates in Wuhan in 2002, 2003, and 2004. The authors did not explain these high-death-rate years in terms of any known phenomena and did not hazard a hypothesis that might explain this situation.

POLLUTANT MONITORING AND EXPOSURE ESTIMATION IN WUHAN

Regional levels of PM_{10}, SO_2, and NO_2 appear to vary temporally in a similar fashion (site-to-site Pearson correlations ranged between 0.59–0.84 for NO_2 to 0.83–0.97 for PM_{10}; see Table C.14 of the Qian Investigators' Report), suggesting that the averaged concentrations will accurately reflect the daily variation in those pollutant concentrations. However, given that data from only one O_3 monitor was used, we are unable to assess if that is also the case for O_3. While, having only one O_3 monitor is a weakness of this study, usually O_3 is regionally less variable than other

pollutants, and the consistency in the variability of other pollutant concentrations throughout the region would suggest that observed O_3 would be reasonably well represented by the available data.

Correlations between pollutant concentrations were the highest for NO_2 with PM_{10} and NO_2 with SO_2 (0.59 and 0.57, respectively; see Table 6 in the Qian Investigators' Report), but are moderate. This moderate correlation would suggest that these pollutants share some sources (possibly traffic and industrial emissions).

As in the other PAPA reports, there was only a very brief characterization of the regional sources and dynamics of the pollutants. Further, there was no discussion of how specific sources may have impacted specific monitoring locations, which would have allowed for better interpretation of the monitor data.

METHODS FOR STATISTICAL ANALYSIS

There were some complexities of the statistical analysis in the Wuhan study that made it hard to follow and to be sure of the properties of the models. First, the investigators applied many approaches to the selection of covariate terms, all of which seemed to address properties of estimated residuals, rather than the control of confounding, which was the priority in this study. Nevertheless, the main findings were obtained from the Common Protocol model, and thus are at least comparable with those from the other PAPA studies and many other studies, such as the APHEA studies (Touloumi et al. 1997), using similar approaches.

Second, in order to address two apparently anomalous periods of very high mortality, the investigators fitted additional functions of time for those periods. Though this process may have effectively removed possibly spurious information from these periods, it is hard to be sure of this, and the expedient strategy of simply removing these time periods would surely have achieved this more clearly. This alternative analysis was done as a sensitivity analysis for the main effects (and showed results similar to the main analysis), but not for the highlighted temperature interactions.

The analyses of the sensitivity of key results to degrees of freedom in the time smoothers (Qian Investigators' Report Figures 8, 11, 12, and E.1; up to 12 df/year) were fairly reassuring, with little sensitivity identified from 6 df per year, which was used for the analyses of all natural mortality (Qian Investigators' Report Table 3). There was greater sensitivity to the inclusion of lags for temperature additional to the default lag 0 (Qian Investigators' Report Figures 13, and 14; lag 1–2 day mean and both lag 1–2 and 3–7 day means) for NO_2 and SO_2 effects — though PM_{10} effects (Figure 9) were robust. For example, the NO_2 effect estimates for all natural mortality were reduced from about 2% in the default model to about 1% in the model using lag 1–2 day mean, and the effect estimates were marginally statistically significant with both additional lagged temperature terms (lag 1–2 and 3–7 day means). The SO_2 effect estimate was reduced from 1.2% to 0.6%, and the O_3 from 0.3% to 0.1% (Qian Investigators' Report Table E.1).

A special focus of this study was whether pollution effects were different in the very hot weather experienced in Wuhan summers (or in cold weather in winter). The statistical approach to this, which comprised using interaction terms reflecting additional increments of mortality per unit of pollutant in hot weather in addition to the core model terms used for the main effects analysis, was reasonable. However, much depends in such analyses on whether the main effects of temperature have been adequately captured. If not, apparent modification may reflect residual confounding from heat. The absence of an assessment of whether the temperature main effect model was capable of capturing the temperature effect in the data makes this approach particularly hard to evaluate. Furthermore, no analyses of the sensitivity of the temperature–pollutant interactions to other model terms are presented. In particular, a sensitivity analysis that included additional lags in the main effect of temperature would have been helpful.

ASSESSMENT OF EPIDEMIOLOGIC ANALYSIS

Features of Wuhan (Population, Sources, Meteorology, and Pollutant Concentrations)

As described by Qian and coworkers, Wuhan is a relatively large city and therefore experiences a large number of deaths per day (61 deaths per day on average). Relative to most cities in the United States and Western Europe, the age distribution of the population is somewhat skewed toward the young, as is the distribution for age at death.

Concentrations of air pollutants in Wuhan were high relative to those typically measured in Western cities. A special feature of Wuhan is the very hot temperatures in the summer, with a maximum 24-hour average temperature of 36°C; peak temperatures were undoubtedly higher. The authors exploited this extreme weather by investigating whether the effects of the pollutants were larger on hot days (see section below). During the summer in Wuhan when temperatures were at their highest, daily O_3 concentrations were higher than in other seasons of the year, as expected, but daily PM_{10} concentrations and death counts were lower than in other seasons (Qian Investigators' Report Figures 5 and 7).

Pollutant-Specific Effects and Their Robustness

As described earlier, in the Wuhan time-series study, associations between pollutant concentrations and health effects in single-pollutant models (i.e., those not adjusted for other pollutants) were observed for PM_{10}, NO_2, and SO_2, but not for O_3, though the upper confidence limit for the impact of O_3 on mortality (0.63% per 10 μg/m^3; see Investigators' Report Table 12) was above that found in a recent U.S. study using the National Mortality, Morbidity, and Air Pollution Studies (NMMAPS) database (Bell 2004). Aside from lack of power, it is not clear why health effects associated with O_3 were not observed in Wuhan, apart from those present on high temperature days (see section below). O_3 effects, more than those of other pollutants, might be expected to be affected by population time–activity patterns. If residents of Wuhan spend more time indoors with the windows closed, for example, the effects of O_3 might be expected to be less obvious. Time-series studies have found substantial heterogeneity in O_3 effects across cities, as demonstrated in NMMAPS (Bell 2004). Reasons for this heterogeneity are not understood, but the presence of heterogeneity suggests less weight should be placed on single-city results.

None of the main pollutant effects were very sensitive to differences in model specifications due to the degree of smoothing for time or to the choice of regression spline (natural or penalized), when using at least 6 df/year. However, as was seen in the other PAPA studies, pollutant effects were sensitive to how the effects of meteorology were modeled, as noted earlier. The effects of PM_{10} were only slightly attenuated by the inclusion of longer lags for humidity and temperature, but the effects of NO_2 and SO_2 were greatly attenuated, often no longer showing any effect. These observations raise the question as to which effect estimates are the most credible — those with more aggressive control for meteorology or those without. The adequate control of temperature is particularly important in a city subject to temperature extremes such as those found in Wuhan. The question of adequate control for temperature is discussed more fully in the Integrated Discussion (in Part 5 of this volume).

In two-pollutant models, the associations of both PM_{10} and SO_2 (Qian Investigators' Report Tables 10 and 15) with daily total all natural and cardiovascular mortality were greatly attenuated with the inclusion of an NO_2 term in the models. The estimated effects of NO_2 (Qian Investigators' Report Table 14) were only somewhat attenuated with the inclusion of PM_{10} in the models. At face value, these findings suggest that the effects of both PM_{10} and SO_2 were confounded by NO_2, and that the pollutant effects in Wuhan on daily mortality are largely those due to NO_2. This issue is also addressed in the Integrated Discussion.

Health Endpoints

The Wuhan study used health endpoints commonly employed in time-series studies throughout the world. As is often seen in time-series mortality studies, the effect estimates in the stratum of cardiovascular deaths for the Wuhan study were larger than those for all natural mortality, and the effect estimates for the category of respiratory deaths were generally higher than those of any other category of death (Qian Investigators' Report Table E.1). As was also the case in the other PAPA cities, short-term increases in pollutant concentrations were associated with increases in nonaccidental, non-cardiopulmonary mortality. However, we wouldn't expect deaths in this stratum to be associated with air pollution exposure if cardiovascular and pulmonary deaths are properly categorized. The authors did not report any findings for accidental death, another cause-of-death category not expected to be associated with air pollution. A null association here would have been reassuring and would have implied that the study methods were not creating biased results. The scientific implications of the findings relating to non-cardiopulmonary causes of death are not clear. Further discussion of this issue is included in the Integrated Discussion (in Part 5 of this volume).

Interaction Between Pollutants and High Temperature

The finding of higher effects on mortality per unit concentration of PM_{10} on hot versus normal days (heat–PM interaction) is of particular interest within the context of impending climate change in which temperatures are likely to increase. However, there are several reasons to be cautious in interpreting this result. First, as noted in the evaluation of the methods above, unbiased estimation of interactions depend critically on correctly capturing in the model the main effect of the two exposures under investigation — here, pollution and heat. Though the model includes temperature in a spline form, as is fairly conventional in air pollution epidemiology, this is no guarantee that this function will adequately capture the impact of heat on mortality, particularly in a city with such temperature extremes. Temperature effects are typically larger than pollution effects, so the potential for residual confounding of pollutant effects and their interactions is an important concern. Analyses of the sensitivity of the heat–PM interaction to the lag and functional form of the main temperature model might reassure, but are not presented. The main effect of temperature alone is also not presented. Qian Investigators' Report Figure 18 comes close to showing the direct temperature effects, but the shape of the mortality/temperature plot is influenced by stratification of variables other than temperature, which complicates its

interpretation. A better awareness of the size of the heat effect would help in assessing likely residual confounding by heat in the estimate of heat–PM interaction.

Other residual confounding relations could also behave differently on hot days relative to normal days, distorting interactions. The incomplete reflection in the model of the abnormal mortality period that occurred in a period of extremely hot weather might be one such source of residual confounding. Thus, though the heat–PM_{10} interaction merits further investigation, it comprises suggestive rather than strong evidence for a greater impact of PM_{10} on mortality on hot versus normal days. If the interaction were to be causal, the fact that in Wuhan hot days were accompanied by lower concentrations of PM_{10} than on normal days (Qian Investigators' Report Table 18) is reassuring with respect to the possible impacts of higher temperatures on pollution-caused deaths.

Sensitivity Analysis

The investigators in Wuhan performed an additional sensitivity analysis: they took the opportunity to assess the impact of the change in cause-of-death coding from ICD-9 to ICD-10 during the study period. They found that there was good concordance between the two coding schemes and excellent coding practices before and after the change. As a result, the particular coding scheme used had negligible impact on their estimates of effect, which is reassuring.

CONCLUSIONS

The Wuhan study will assist policymakers to improve public health policy on air pollution by providing estimates of the impacts of pollution on daily mortality in a city with unusually widely ranging and occasionally extreme daily pollutant exposure levels and temperatures. The Committee believes that, although the uncertainties are greater than is reflected in the confidence intervals, the existence of pollutant effects on mortality is a robust finding. For PM_{10}, at least, the effect estimates are consistent with those found in other cities in China, North America, and Europe.

The interpretation of results as to which specific pollutants are more toxic and as to the apparent modification of the pollutant effect by temperature should be more cautious. Though these results provide useful suggestive evidence, these subtle patterns are more likely to be distorted by residual biases. The resolution of the key questions these results raise will require future research in which Wuhan, with its unusual climate and pollutant patterns, may play an important part.

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