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# Public Health and Air Pollution in Asia (PAPA): Key Results from Bangkok, Hong Kong, Shanghai, and Wuhan

Includes Individual-City and Combined Results Plus an Editorial
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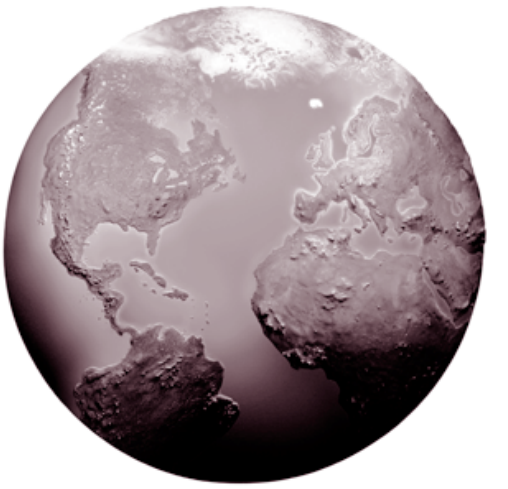

# Public Health and Air Pollution in Asia (PAPA): Key Results from Bangkok, Hong Kong, Shanghai, and Wuhan

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# Asia: Changing Times and Changing Problems

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Frank E. Speizer


Aaron Cohen


Sumi Mehta

Asia is currently experiencing rapid increases in industrialization, urbanization, and vehicularization. As a result, emission trends (e.g., energy, fuel, vehicle use), population trends (e.g., degree of urbanization, urban population growth, city size), health trends (e.g., age structure, background disease rates), and other important factors (e.g., broad changes in regulatory approaches, improvements in control technology) will influence the extent to which exposure to air pollution affects the health of the Asian population over the next several decades. Because the effects on air quality of recent, rapid development are clearly apparent in many of Asia's cities and industrial areas, government decision makers, the private sector, and other local stakeholders are increasingly raising concerns about the health impacts of urban air pollution. Major Asian cities, such as Shanghai (China), Delhi (India), Ho Chi Minh City (Vietnam), and Manila (Philippines), now experience annual average levels of respirable particles [particulate matter ≤ 10 μm in aerodynamic diameter ($PM_{10}$)] in excess of the World Health Organization's (WHO) newly revised world air quality guideline of 50 μg/m$^3$ (WHO 2006).

The health impacts in the region are already estimated to be substantial. The WHO (2002) estimated that urban air pollution contributed to approximately 800,000 deaths and 6.4 million lost life-years worldwide in 2000, with two-thirds of these losses occurring in rapidly urbanizing countries of Asia. These estimates were made using the results of U.S. studies of long-term exposure to air pollution because such studies have not yet been conducted in the developing countries of Asia, where health, health care, exposure to pollution, and socioeconomic circumstances still differ markedly from the United States. This contributes considerable uncertainty to these and other recent estimates of health impacts of air pollution (Cohen et al. 2004).

High-quality, credible science from locally relevant studies is essential to address the substantial air pollution challenges in Asia. Such studies will be critical in helping decision makers decide which policies are most likely to result in public health benefits. Although the number of published studies on the health effects of air pollution in Asia has grown nearly exponentially over the past quarter century, with > 400 reports in the peer-reviewed literature [Health Effects Institute (HEI) 2008], few coordinated, multicity time-series studies have been conducted comparable to the robust and consistent results in the United States and Europe (Katsouyanni et al. 2001; Samet et al. 2000). The Public Health and Air Pollution in Asia (PAPA) studies in Hong Kong, Shanghai, and Wuhan, China, and Bangkok, Thailand, published in this issue of *Environmental Health Perspectives* (Kan et al. 2008; Qian et al. 2008; Vichit-Vadakan et al. 2008; Wong et al. 2008a, 2008b), comprise the first coordinated multicity analyses of air pollution and daily mortality in Asia. These studies, designed and conducted by local investigators in concert with local air pollution and public health officials and international experts, explored key aspects of the epidemiology of exposure to air pollution in each location, providing additional insight about how factors such as weather (particularly high temperatures) and social class might modify the air pollution relative risk. Although clearly relevant to contemporary Asian conditions, these results also have global relevance.

The studies were conducted using the same types of mortality and air pollution data used in time-series studies throughout the world, and with methodologic rigor that matches or exceeds that of most published studies, including formal quality control in the form of detailed standard operating procedures for data collection and analysis, and external quality assurance audits of the data overseen by the funding organization. These studies also benefited from recent efforts to strengthen and refine methods for the analysis of time-series data; as a result they are on a par methodologically with the most recent U.S. and European analyses (HEI 2003).

These five studies provide a relatively consistent, if limited, picture of the acute mortality impact of current ambient particulate air pollution in several large metropolitan areas in East and Southeast Asia. Wong et al. (2008b) report that a 10-μg/m$^3$ increase in $PM_{10}$ level was associated with a 0.6% (95% confidence interval, 0.3–0.9) increase in daily rates of all natural-cause mortality, estimates comparable to or greater than those reported in U.S. and European multicity studies. Interestingly, these proportional increases in mortality are seen at levels of exposure several times higher than those in most large Western cities (mean levels, 51.6–141.8 μg/m$^3$), and in each city except Shanghai, the pattern of the exposure–response functions appear linear over a fairly large range of ambient concentrations up to and sometimes > 100 μg/m$^3$.

Although only four cities were studied, these results may begin to allay concerns regarding the generalizability of the results of the substantial, but largely Western, literature on the effects of short-term exposure to air pollution. The results, which are broadly consistent with previous research (HEI 2004), suggest that neither genetic factors nor longer-term exposure to highly polluted air substantially modify the effect of short-term exposure on daily mortality rates in major cities in developing Asia. This provides support for the notion, implicit in the approach taken in the WHO's world air quality guidelines (Krzyzanowski and Cohen 2008), that incremental improvements in air quality would be expected to improve health, even in areas with relatively high ambient concentrations.

Health impacts in cities in developing countries of Asia result from exposures to a mixture of pollutants, particles, and gases, which are derived in large measure from combustion sources (Harrison 2006; Wong et al. 2008b). This is, of course, no different from in Europe and North America, but the specific sources and their proportional contributions are different, with open burning of biomass and solid waste materials, combustion of lower-quality fuels including coal, and two- and three-wheeled vehicles contributing a larger share in Asia. Time–activity patterns, building characteristics, and proximity of susceptible populations to pollution sources also differ in ways that may affect human exposure and health effects (Janssen and Mehta 2006). Our current knowledge of these issues is rudimentary, and additional research is clearly needed to inform effective and sustainable control strategies. From past experience in the West and current evidence in Asia, substantial increases in the combustion of fossil fuels for power generation and transportation in developing Asia will have important consequences for human health and environmental quality in Asia and beyond. Effective approaches to pollution control and reduction do exist, and investment in these approaches need not necessarily impede economic growth. Therefore, developing countries of Asia may be able to avoid increased environmental degradation and associated health impacts while reducing poverty and providing

economic security for their populations (Center for Science and the Environment 2006).

Thirty million people currently live in the four cities studied, so even the small proportional increases in daily mortality rates imply large numbers of excess deaths. That said, air pollution is but one of many factors that affect the health of people in developing Asia, and, unfortunately, not even the most important one (Ezzati et al. 2002). Nonetheless, the substantial health impacts of exposure to air pollution should be of concern to public health policy makers faced with difficult decisions in transportation and energy policy. Given current predictions of even more accelerated urbanization in the regions, there will be an increasing need for more extensive monitoring of urban air quality designed to support health effects studies and impact assessments, and a corresponding need for more highly trained professionals in air quality monitoring, exposure assessment, and environmental epidemiology.

Strategic planning for future research is also needed. Although our ability to draw firm conclusions from results in four cities is limited, the methods of Wong et al. (2008b) can be replicated in additional cities across the regions. In some cases, nonmortality outcomes, such as hospital admissions, may also be addressed, enabling policy makers to better quantify the health impacts of air pollution. However, while time-series studies such as the PAPA studies will continue to be important potential drivers of environmental and public policy, additional study designs, such as cohort studies—similar to the U.S. American Cancer Society (Pope et al. 2002) and Six Cities (Laden et al. 2006) studies—are needed in Asian populations to estimate effects of long-term exposure on annual average mortality and life expectancy, the metrics that may be the most meaningful and policy relevant to decision makers. These kinds of studies will require the building of multidisciplinary teams of investigators, with adequate long-term commitment of resources to work in collaboration with governmental officials, their industrial counterparts, and local stakeholders. The PAPA program is one model of how such resources can be brought together to support such an effort.

*The views expressed in this paper are those of the authors and do not necessarily reflect the views of the Health Effects Institute (HEI) or its sponsors; however, F.E.S is chairman of the HEI International Scientific Oversight Committee that was responsible for guiding the conduct and providing input to the investigators as needed.*

*The authors declare they have no competing financial interests.*

**Frank E. Speizer**
Channing Laboratory
Harvard Medical School
Boston, Massachusetts
E-mail: frank.speizer@channing.harvard.edu

**Aaron Cohen**
**Sumi Mehta**
Health Effects Institute
Boston, Massachusetts

*Frank E. Speizer is the E.H. Kass Professor in Medicine at Harvard Medical School and professor of Environmental Science at the Harvard School of Public Health. He has conducted research in air pollution health effects for more than 40 years and was one of the principal investigators in the Harvard Six Cities Study.*

*Aaron Cohen, a principal scientist, and Sumi Mehta, a senior scientist, both at the Health Effects Institute, manage an international program of epidemiologic research on the health effects of air pollution. They also are involved in scientific program development.*

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# High Temperatures Enhanced Acute Mortality Effects of Ambient Particle Pollution in the "Oven" City of Wuhan, China

*Zhengmin Qian,[1,2] Qingci He,[3] Hung-Mo Lin,[1,4] Lingli Kong,[3] Christy M. Bentley,[1] Wenshan Liu,[5] and Dunjin Zhou[6]*

[1]Department of Public Health Sciences, Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA; [2]Geisinger Center for Health Research, Danville, Pennsylvania, USA; [3]Wuhan Academy of Environmental Science, Wuhan, China; [4]Mount Sinai School of Medicine, New York, NY, USA; [5]Wuhan Environmental Monitoring Center, Wuhan, China; [6]Wuhan Centres for Disease Prevention and Control, Wuhan, China

**Background:** We investigated whether the effect of air pollution on daily mortality is enhanced by high temperatures in Wuhan, China, using data from 2001 to 2004. Wuhan has been called an "oven" city because of its hot summers. Approximately 4.5 million permanent residents live in the 201-km$^2$ core area of the city.

**Method:** We used a generalized additive model to analyze pollution, mortality, and covariate data. The estimates of the interaction between high temperature and air pollution were obtained from the main effects and pollutant–temperature interaction models.

**Results:** We observed effects of consistently and statistically significant interactions between particulate matter ≤ 10 μm ($PM_{10}$) and temperature on daily nonaccidental ($p$ = 0.014), cardiovascular ($p$ = 0.007), and cardiopulmonary ($p$ = 0.014) mortality. The $PM_{10}$ effects were strongest on extremely high-temperature days (daily average temperature, 33.1°C), less strong on extremely low-temperature days (2.2°C), and weakest on normal-temperature days (18.0°C). The estimates of the mean percentage of change in daily mortality per 10-μg/m$^3$ increase in $PM_{10}$ concentrations at the average of lags 0 and 1 day during hot temperature were 2.20% (95% confidence interval), 0.74–3.68) for nonaccidental, 3.28% (1.24–5.37) for cardiovascular, 2.35% (–0.03 to 4.78) for stroke, 3.31% (–0.22 to 6.97) for cardiac, 1.15% (–3.54% to 6.07) for respiratory, and 3.02% (1.03–5.04) for cardiopulmonary mortality.

**Conclusions:** We found synergistic effects of $PM_{10}$ and high temperatures on daily nonaccidental, cardiovascular, and cardiopulmonary mortality in Wuhan.

**Key words:** air pollution, China, health effect, mortality, temperature. *Environ Health Perspect* 116:1172–1178 (2008). doi:10.1289/ehp.10847 available via *http://dx.doi.org/* [Online 9 July 2008]

Extreme temperatures are associated with increased daily mortality in many regions of the world (Patz and Khaliq 2002). Because human activity is likely to increase overall global average temperatures, research efforts have focused on the health effects of exposure to high temperatures and heat waves in summer. In the United States, increased mortality during high-temperature days has been extensively investigated. Semenza et al. (1996) reported that a heat wave in Chicago, Illinois, in 1995 was associated with an increase in the death rate among socially isolated people who had no air conditioning. In studies of multiple U.S. cities, similar results were reported (Curriero et al. 2002). In Europe, excess mortality during high-temperature days has also been noted. Le Tertre et al. (2006) also reported an association between the 2003 heat wave in France and increases in all causes of mortality in nine French cities. Stafoggia et al. (2006) explored vulnerability to heat-related mortality in four Italian cities: Bologna, Milan, Rome, and Turin. The populations particularly vulnerable to high summer temperatures were the elderly, women, widows and widowers, those with particular medical conditions, and those in nursing homes and health care facilities.

Air pollution is also associated with increased daily mortality (Pope 2000). A large number of daily mortality time-series analyses have provided sufficiently convincing evidence that nonaccidental mortality, including cardiopulmonary mortality, is associated with ambient particulate matter (PM) exposure in the United States (Ostro et al. 2007), Canada (Burnett et al. 2000), Rome (Forastiere et al. 2007), China (Kan et al. 2007), Korea (Lee et al. 2000), Greece (Katsouyanni et al. 1997), and Chile (Cakmak et al. 2007). The estimated effect is generally in the range of 1.0–8.0% excess deaths per 50-μg/m$^3$ increments in 24-hr average concentrations of particulate matter ≤ 10 μm in aerodynamic diameter ($PM_{10}$) (Schwartz and Zanobetti 2000).

Although the independent impacts of high temperature and air pollution on daily mortality have been widely explored, few studies have examined the interaction between high temperature and air pollution (Samet et al. 1998). Investigating the effects of the synergy between air pollution and high temperature on mortality, although desirable, is difficult, because a suitable study site is not easily available. The Chinese city of Wuhan, however, provides an opportunity to examine these synergistic effects; it has been called an "oven" city because of its extremely hot summers. Previous studies in Wuhan (He et al. 1993; Qian et al. 2004) have shown high air pollution levels, with concentration ranges wider than those reported in the published literature for other locations. Therefore, we tested the hypothesis that temperature extremes modify the mortality effects of air pollution.

## Methods

*Study area and population.* Wuhan is the capital of Hubei Province, which is located in the middle of the Yangzi River delta, at 29°58′–31°22′ north latitude and 113°41′–115°05′ east longitude. Its population is approximately 7.5 million people, of whom approximately 4.5 million reside in nine urban core districts within an area of 201 km$^2$. Wuhan has a subtropical, humid, monsoon climate with a distinct pattern of four seasons. Its average daily temperature in July is 37.2°C, and the maximum daily temperature often exceeds 40°C. The major industries in Wuhan include ferrous smelters, chemical plants, power plants, and machinery plants. The major sources of air pollution in the city are motor vehicles and the burning of coal for domestic cooking, heating, and industrial processes.

*Data sources.* Mortality data from 1 July 2000 to 30 June 2004 were obtained from the Wuhan Centres for Disease Prevention and Control (WCDC). The government requires that a decedent's family obtain a death certificate from a hospital or a local community clinic to remove the deceased person from the government-controlled household registration. The local WCDC issues two copies of the death certificate according to the certificate from the hospital or the clinic. One copy is submitted to the public safety department to stop the decedent's address registration, and the other copy is used for the cremation.

The WCDC electronically archives all death certificates. In 1992, the WCDC became the first center in China to standardize

Address correspondence to Z. Qian, Geisinger Center for Health Research, M.C. 44-00, Danville, PA 17822 USA. Telephone (570) 214-6594. Fax: (570) 214-5170. E-mail: zqian1@geisinger.edu

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its system for mortality data collection. The system's requirements are as follows: *a*) mortality data must be validated four times per year; *b*) death events collected from the WCDC must conform with those collected from the Wuhan Police Department; *c*) no data may be missing from any death certificate; *d*) unclear causes and diagnosis may not constitute > 2% of deaths in urban districts; and *e*) a correct coding rate of > 98% must be achieved for cause-specific deaths. For deaths that occurred before 1 January 2003, the *International Classification of Disease, Ninth Revision* [ICD-9; World Health Organization (WHO) 1978] codes were applied; for deaths that occurred after 31 December 2002, ICD-10 (WHO 1993) codes were applied. Total mortality was divided into the following major causes: nonaccidental mortality (ICD-9 codes 1–799; ICD-10 codes A00–R99), cardiovascular diseases (ICD-9 codes 390–459; ICD-10 codes I00–I99), stroke (ICD-9 codes 430–438; ICD-10 codes I60–I69), cardiac diseases (ICD-9 codes 390–398 and 410–429; ICD-10 codes I00–I09 and I20–I52), respiratory diseases (ICD-9 codes 460–519; ICD-10 codes J00–J98), and cardiopulmonary diseases (ICD-9 codes 390–459 and 460–519; ICD-10 codes I00–I99 and ICD-10 J00–J98). The Human Subject Protection Office of the Penn State College of Medicine approved the current study protocol.

Pollution data were collected by the Wuhan Environmental Monitoring Center (WEMC) and certified by the U.S. Environmental Protection Agency. Daily concentrations of $PM_{10}$, sulfur dioxide, nitrogen dioxide, and ozone (8-hr mean concentrations, 1000–1800 hours) were collected for the study period. The monitoring system strictly followed the quality assurance/quality control procedure set by the State Environmental Protection Administration of China (1992). Briefly, the WEMC conducts regularly scheduled performance audits and precision checks on the air-monitoring equipment. Quarterly performance audits are also conducted to assess data accuracy. $PM_{10}$ measurements were collected using $PM_{10}$ beta attenuation mass monitors, (model 7001); $SO_2$ measurements were collected using an ultraviolet fluorescence $SO_2$ analyzer (model 4108); $NO_2$ measurements were collected using a chemiluminescent $NO_2$ analyzer (model 2108); and $O_3$ measurements were collected using an ultraviolet photometry $O_3$ analyzer (model 1008), all from Dasibi Environmental Corporation (Glendale, CA, USA). Meteorologic data were provided by the Wuhan Meteorological Administration.

***Statistical methods.*** We used quasi-likelihood estimation within the context of the generalized additive models (GAMs) to model the natural logarithm of the expected daily death counts as a function of the predictor variables (Hastie and Tibshirani 1990). We examined the effect estimates for each pollutant at 0-, 1-, 2-, 3-, and 4-day lags, and at lag 0–1 day and lag 0–4 day average concentrations prior to the death events. In general, the largest pollutant effects were observed at the lag 0–1, where pollution concentrations were evaluated at the average of the day of death (lag 0) and 1 day before death (lag 1). Therefore, for purposes of this study we focused on the results of the lag 0–1 model. All model analyses were performed using R, version 2.5.0, using the mgcv package, 1.3-24 (The R Foundation for Statistical Computing 2007).

There were two steps in the model building and fit: development of the best base model (without a pollutant) and development of the main model (with a pollutant). The latter was achieved by adding the air pollution variable(s) to the final and best cause-specific base model, assuming a linear relationship between the logarithmic mortality count and the air pollutant concentration. To obtain the best base model, the GAM analyses were performed covering two major areas. First, we controlled for potential confounding of yearly, seasonal, and subseasonal variations and for other time-varying influences on mortality. To begin, we included indicators for days of the week to take into account the change in traffic volume between workdays and weekends. We then regressed the natural logarithm of the daily death counts on a day sequence to adjust for time trends using either natural splines (ns) or penalized splines (ps). Furthermore, visual inspection of the mortality time-series showed two peaks of death counts over the two periods 28 July–3 August 2003 (sum03) and 1 December–31 December 2003 (win03). We added a factor variable for the three periods (sum03, win03, and others) and performed local smoothing by specifying the "by" option for these three periods to control for the extreme peaks of death counts. Second, we controlled for potential confounding of relevant weather variables, which is important during unusually high and low temperatures in Wuhan. We controlled for weather variables using *a*) indicator variables for extremely hot days, cold days, and humid days; and *b*) ns or ps for the temperature and humidity, respectively. The extremely hot and cold days were defined as those days on which the highest or lowest daily average temperatures were > 95th percentile or < 5th percentile of the 4 years of data, respectively (Dockery et al. 1992). The 5th and 95th percentiles for temperature were 3.6 and 31.7°C.. Similarly, the extremely humid days were those days with daily average relative humidity > 95th percentile of the 4 years of data. The goal in the previous two steps was to obtain conservative estimates on the subsequent pollution mortality associations.

Taking into account the literature review and the common protocol of the Health Effects Institute's program of the Public Health and Air Pollution in Asia, we used four competing approaches to determine the appropriate degrees of freedom (df) for the time and weather in developing the best base model for each cause-specific mortality model (Curriero et al. 2002; Dominici et al. 2003). These include two ns methods that used the fixed df, the sequential ns method, and the ps method, where the former three ns methods were parametric-based regression splines and always used 2 df and 3 df for the local smoothers for sum03 and win03, respectively. For the two fixed-df models, we considered 6 and 8 df/year for time, 3 and 4 df for temperature, and 3 and 4 df for humidity over the entire 4-year study period. For the sequential method, we started with a reduced model (only days of week, extreme weather indicators, and local smoothing terms). We tried 3–8 df/year for the time and then chose the df that had the smallest sum of the absolute partial autocorrelation values over a 30-day lag period. Next we added temperature to the above model using 2–4 df. We repeated this process for relative humidity after including temperature, time trend, days of week, and extreme weather indicators. We ran the ps model to select the optimal df for overall time trend, local time intervals, temperature, and relative humidity. We initialized the df as 8 df/year for time, 3 df for sum03, 3 df for win03, and 3 df for both temperature and relative humidity. We observed that the local smoothing df remains the same or within 1–2 df differences from the dfs used in the sequential method for various cause-specific mortality. The criteria for selecting the best-fitting model are as follows: *a*) the absolute value of the partial autocorrelation < 0.1 for all 30-day lags; and *b*) the smallest sum of the absolute partial autocorrelation values over a 30-day lag period.

To address whether estimated effects are valid and whether they are strongly influenced by different model specifications during the modeling process, we conducted a series of sensitivity analyses in two areas. The first area concerns different smoothing approaches for time, temperature, and humidity. These included *a*) alternating smoothing order in the sequential method from time, temperature, and humidity to temperature, humidity, and time; *b*) using fixed df for time, temperature, and humidity (e.g., 6 df for time/year, 3 df for temperature, and 3 df for humidity; and 8 df for time/year, 4 df for temperature, and 4 df for humidity); and *c*) using the ps approach. The second area concerns model specifications, where the best main models were fitted alternatively by *a*) adding influenza epidemics; *b*) adding an indicator for the period of ICD-10 use; *c*) removing Wuhan, the most

industrialized district; *d*) removing extreme temperature data; *e*) redefining extreme temperature; and *f*) adding the lag climate variable

Last, we redefined the temperature groups using different percentile cutoffs of the temperature ranges (3rd, 7th, 10th, and 15th percentiles) to determine whether the effects observed using the 5th percentiles were significantly changed.

We used several approaches to investigate the validity of the linearity assumption for each air pollutant. First, we replaced the linear term of the pollutant concentrations with a smooth function with 3 df using ns. 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 resembles a straight line. Next, we performed piecewise regression models by allowing different slopes of pollutant concentrations before and after a cutoff point. The cutoff points of $PM_{10}$ were tested from zero to 150 μg/m$^3$ in 25-μg/m$^3$ increments. The best piecewise regression model was the one in which the cutoff point minimized the generalized cross-validation value. In general, assuming the linearity of air pollution effects on the logarithm of mortality appears to be appropriate.

To investigate the synergetic effects between air pollution and temperature, our

**Table 1.** Distributions of mean daily ambient air pollutants (μg/m$^3$) and weather variables by temperature[a] in Wuhan, China, July 2001–June 2004.

| Pollutant | Normal temperature | | Low temperature | | High temperature | |
|---|---|---|---|---|---|---|
| | Days (*n*) | Mean ± SD | Days (*n*) | Mean ± SD | Days (*n*) | Mean ± SD |
| $PM_{10}$ | 1,312 | 145.7 ± 64.6 | 73 | 117.3 ± 49.5 | 73 | 96.3 ± 27.9 |
| $O_3$ | 1,265 | 87.4 ± 47.5 | 72 | 51.5 ± 24.5 | 49 | 91.9 ± 41.8 |
| $SO_2$ | 1,311 | 39.4 ± 25.4 | 73 | 50.3 ± 26.7 | 73 | 23.8 ± 10.2 |
| $NO_2$ | 1,311 | 52.9 ± 18.7 | 73 | 51.2 ± 17.8 | 73 | 32.5 ± 6.2 |
| Daily mean temperature (°C) | 1,315 | 18.0 ± 8.2 | 73 | 2.2 ± 1.3 | 73 | 33.1 ± 0.9 |
| Daily mean relative humidity (%) | 1,315 | 74.4 ± 12.4 | 73 | 75.3 ± 16.0 | 73 | 64.7 ± 5.6 |

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

**Table 2.** Correlations and trends in measured ambient air pollutants by temperature in Wuhan, China, July 2001–June 2004.

| Pollutant (μg/m$^3$) | No. of monitoring stations | Range of mean values between stations | Coefficient of variation of daily mean (%) | Range of Pearson correlation coefficients between monitoring stations | Mean of daily means | |
|---|---|---|---|---|---|---|
| | | | | | Mean | Average annual change[a] |
| $PM_{10}$ | | | | | | |
| Normal temperature | 5 | 116.9–166.1 | 44.3 | 0.83–0.97 | 145.7 | –4.5 |
| Low temperature | 5 | 95.5–126.6 | 42.2 | 0.76–0.97 | 117.3 | 4.3 |
| High temperature | 5 | 72.7–118.6 | 28.9 | 0.50–0.93 | 96.3 | –1.5 |
| $O_3$ | | | | | | |
| Normal temperature | 1 | NA | 54.3 | NA | 87.4 | –2.8 |
| Low temperature | 1 | NA | 47.7 | NA | 51.5 | 4.6 |
| High temperature | 1 | NA | 45.5 | NA | 91.9 | –3.0 |
| $SO_2$ | | | | | | |
| Normal temperature | 4 | 32.8–45.9 | 64.4 | 0.64–0.84 | 39.4 | 3.3 |
| Low temperature | 4 | 41.3–58.7 | 53.0 | 0.61–0.87 | 50.3 | 4.0 |
| High temperature | 4 | 17.4–28.1 | 42.9 | 0.27–0.78 | 23.8 | 2.6 |
| $NO_2$ | | | | | | |
| Normal temperature | 5 | 36.3–64.8 | 35.3 | 0.57–0.84 | 52.9 | 2.1 |
| Low temperature | 5 | 37.6–61.9 | 34.8 | 0.69–0.86 | 51.2 | 3.3 |
| High temperature | 5 | 22.3–43.2 | 19.1 | 0.11–0.66 | 32.5 | 1.3 |

NA, not applicable.
[a]Calculated from a linear regression model.

**Table 3.** Daily mortality in Wuhan, China, by cause of death and temperature, July 2001–June 2004.

| Underlying cause of death | Total no. of deaths | No. of days with no deaths | Mean | Variance | Variance/mean | Percentile | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Minimum | Maximum | 25th | 50th | 75th |
| Nonaccidental | | | | | | | | | | |
| Normal temperature | 78,666 | 0 | 59.82 | 216.23 | 3.61 | 25 | 213 | 50 | 58 | 67 |
| Low temperature | 5,839 | 0 | 79.99 | 142.96 | 1.79 | 57 | 107 | 71 | 80 | 88 |
| High temperature | 4,626 | 0 | 63.37 | 562.10 | 8.87 | 40 | 156 | 51 | 56 | 68 |
| Cardiovascular | | | | | | | | | | |
| Normal temperature | 35,684 | 0 | 27.14 | 65.75 | 2.42 | 8 | 67 | 21 | 26 | 32 |
| Low temperature | 2,815 | 0 | 38.56 | 56.78 | 1.47 | 26 | 60 | 33 | 37 | 43 |
| High temperature | 2,124 | 0 | 29.10 | 194.73 | 6.69 | 11 | 94 | 22 | 26 | 32 |
| Stroke | | | | | | | | | | |
| Normal temperature | 22,544 | 0 | 17.14 | 31.24 | 1.82 | 4 | 43 | 13 | 17 | 21 |
| Low temperature | 1,713 | 0 | 23.47 | 25.97 | 1.11 | 14 | 35 | 20 | 23 | 27 |
| High temperature | 1,300 | 0 | 17.81 | 71.27 | 4.00 | 6 | 57 | 13 | 16 | 20 |
| Cardiac | | | | | | | | | | |
| Normal temperature | 10,634 | 2 | 8.09 | 12.09 | 1.50 | 0 | 22 | 6 | 8 | 10 |
| Low temperature | 898 | 0 | 12.30 | 16.88 | 1.37 | 3 | 23 | 9 | 12 | 15 |
| High temperature | 634 | 0 | 8.68 | 25.11 | 2.89 | 2 | 29 | 5 | 8 | 11 |
| Respiratory | | | | | | | | | | |
| Normal temperature | 8,894 | 9 | 6.76 | 32.14 | 4.75 | 0 | 125 | 4 | 6 | 8 |
| Low temperature | 894 | 0 | 12.25 | 15.86 | 1.29 | 5 | 25 | 9 | 13 | 15 |
| High temperature | 499 | 0 | 6.84 | 46.50 | 6.80 | 1 | 56 | 4 | 5 | 8 |
| Cardiopulmonary | | | | | | | | | | |
| Normal temperature | 44,578 | 0 | 33.90 | 137.88 | 4.07 | 11 | 185 | 26 | 32 | 39 |
| Low temperature | 3,709 | 0 | 50.81 | 87.88 | 1.73 | 33 | 78 | 44 | 50 | 56 |
| High temperature | 2,623 | 0 | 35.93 | 345.09 | 9.60 | 15 | 111 | 27 | 32 | 38 |

main models were built to include additional season indicators and two interaction terms between a linear term of air pollution and an indicator of either extreme high temperature or extreme low temperature (the normal temperature serves as the reference). The effect estimates were expressed using a percentage change in the mean number of daily deaths per 10-μg/m$^3$ increments in 24-hr mean concentrations of a pollutant (8-hr mean concentrations for $O_3$). The associated upper and lower 95% confidence limits by weather condition were obtained by taking the exponential of the upper and lower 95% confidence limits of the estimated βs. The overall test of the interaction effects between extreme high and low temperatures and air pollution was performed using the likelihood ratio test with 2 df.

## Results

The daily mean concentrations of $PM_{10}$, $SO_2$, and $NO_2$ were much lower during high-temperature days than during low-temperature and normal-temperature days (Table 1). The 8-hr mean concentrations of $O_3$, as expected, were highest during the high-temperature days. There was great variation in the daily average temperature (33.1°C vs. 2.2°C) but small variation in the daily average relative humidity among the three temperature groups.

There were considerable variations in mean daily levels of pollutants (Table 2). The mean daily concentrations of $SO_2$ and $NO_2$ generally increased during the study period across the three temperature groups. Despite spatial variations in the daily mean concentrations, which were mainly driven by the highest $PM_{10}$ and $SO_2$ concentrations measured at the Wugan station located near a smelter, we found that the distributions of $PM_{10}$ over distances were fairly homogeneous, as shown by the high Pearson correlation coefficients between measurements from the monitoring stations (0.50–0.97). $SO_2$ and $NO_2$ were similarly homogeneously distributed except during the high-temperature days.

We collected information on a total of 89,131 nonaccidental death cases. The daily mean number of nonaccidental deaths was 61, with a maximum of 213 and with a main contribution of cardiopulmonary mortality (daily mean of 35). The majority of individuals died when they were ≥ 65 years of age (71.9%). The mean age of nonaccidental deaths was 69 years, with a range of 0–106 years. Persons ≥ 65 years of age contributed to more than half of the daily deaths for each of the underlying causes of death. The percentage of deaths in the 0–4 year age group was 1.5%. There were only 11 no-death days, all with normal temperature (Table 3). Each variance was greater than the mean, indicating that the mortality data followed the overdispersed Poisson distributions across the three temperature groups, which warrant additional control for weather and temporal trends in the data.

We observed consistent associations between daily mortality and $PM_{10}$, $NO_2$, and $SO_2$ (Qian et al. 2007a, 2007b). In general, using different smoothing approaches did not change the effect estimates significantly, nor did using different model specifications. We also observed a consistent interaction of $PM_{10}$ with temperature (Table 4). The $PM_{10}$ effects were strongest on extremely high-temperature days (daily average temperature, 33.1°C), less strong on extremely low-temperature days (2.2°C), and weakest on normal-temperature days (18.0°C). The estimates of the mean percentage of change in daily mortality per 10-μg/m$^3$ increase in $PM_{10}$ concentrations at the average of lags 0 and 1 day during high temperature were 2.20% [95% confidence interval (CI), 0.74–3.68] for nonaccidental;

**Table 4.** Estimates of the mean percentage of change (95% CI) in daily mortality per 10-μg/m$^3$ increase in pollutants by cause of death and temperature, lag 0–1 day, in Wuhan, China, July 2001–June 2004.

| Cause of death | Temperature | | | *p*-Value |
|---|---|---|---|---|
| | Normal | Low | High | |
| Nonaccidental | | | | |
| $PM_{10}$ | 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 |

**Table 5.** Estimates of the mean percentage of change (95% CI) in daily mortality per 10-μg/m$^3$ increase in $PM_{10}$ concentration by cause of death, temperature, and age, lag 0–1 day, in Wuhan, China, July 2001–June 2004.

| Cause of death, age (years) | Temperature | | | *p*-Value |
|---|---|---|---|---|
| | Normal | Low | High | |
| Nonaccidental | | | | |
| < 65 | 0.23 (–0.10 to 0.56) | 1.78 (0.52 to 3.05) | 2.34 (–0.09 to 4.83) | 0.010 |
| ≥ 65 | 0.41 (0.18 to 0.64) | 0.22 (–0.61 to 1.05) | 2.14 (0.42 to 3.89) | 0.071 |
| Cardiovascular | | | | |
| < 65 | 0.17 (–0.40 to 0.73) | 2.63 (0.67 to 4.63) | 4.32 (0.10 to 8.71) | 0.007 |
| ≥ 65 | 0.44 (0.14 to 0.74) | 0.24 (–0.84 to 1.32) | 3.03 (0.77 to 5.34) | 0.043 |
| Stroke | | | | |
| < 65 | 0.17 (–0.53 to 0.88) | 2.85 (0.34 to 5.42) | 4.54 (–0.79 to 10.16) | 0.031 |
| ≥ 65 | 0.43 (0.07 to 0.79) | 0.11 (–1.22 to 1.45) | 1.83 (–0.83 to 4.57) | 0.489 |
| Cardiac | | | | |
| < 65 | –0.04 (–1.07 to 1.01) | 1.79 (–1.65 to 5.35) | 2.71 (–4.58 to 10.56) | 0.458 |
| ≥ 65 | 0.40 (–0.10 to 0.91) | 0.19 (–1.55 to 1.95) | 3.45 (–0.41 to 7.46) | 0.292 |
| Respiratory | | | | |
| < 65 | –0.35 (–1.85 to 1.18) | –1.13 (–6.33 to 4.35) | –3.42 (–15.82 to 10.80) | 0.856 |
| ≥ 65 | 0.93 (0.38 to 1.50) | 1.30 (–0.57 to 3.20) | 1.76 (–3.03 to 6.78) | 0.852 |
| Cardiopulmonary | | | | |
| < 65 | 0.07 (–0.47 to 0.61) | 1.95 (0.04 to 3.90) | 3.49 (–0.66 to 7.81) | 0.040 |
| ≥ 65 | 0.53 (0.25 to 0.81) | 0.43 (–0.57 to 1.44) | 2.91 (0.74 to 5.12) | 0.052 |

3.28% (1.24–5.37) for cardiovascular; 2.35% (–0.03 to 4.78) for stroke; 3.31% (–0.22 to 6.97) for cardiac; 1.15% (–3.54 to 6.07) for respiratory; and 3.02% (1.03–5.04) for cardiopulmonary mortality. Interestingly, we did not observe consistent stronger temperature effects of modification for the majority of outcomes in the elderly (Table 5). One possible explanation might be that the elderly were more likely to stay inside the house on hot days, avoiding exposure to extreme temperature. For the gaseous pollutants, the only interaction observed was that of $O_3$ on nonaccidental mortality. We found that the estimated $PM_{10}$ effects using the 5th percentile cutoff were generally similar to the effects estimated using the 3rd percentile (Figure 1). Except for respiratory mortality, we observed that the estimated $PM_{10}$ effect decreased with increasing percentile on the high-temperature days. Figure 1 also shows that the relationship of daily mortality with temperature is U-shaped, which is consistent with other studies (Gouveia et al. 2003).

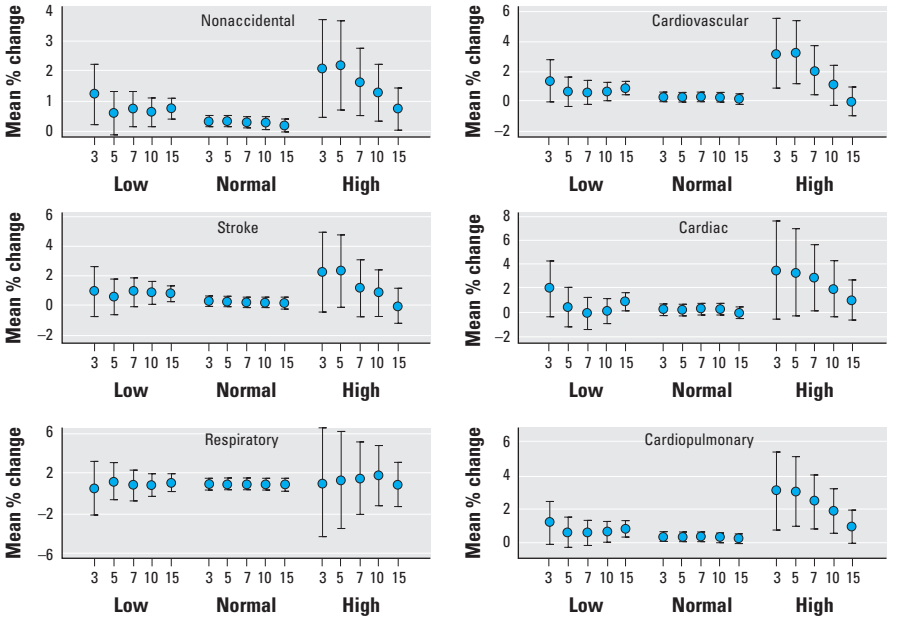


**Figure 1.** Cause-specific mortality plots for $PM_{10}$ stratified by varying percentiles of temperature cutoff points (3, 5, 7, 10, 15) at lag 0–1 day. Values shown are the mean percentage of change in daily mortality per 10-μg/m$^3$ increase in $PM_{10}$ concentration and 95% CI.

**Table 6.** Copollutant regression estimates of the mean percentage of change (95% CI) in daily mortality per 10-μg/m$^3$ increase in $PM_{10}$ concentration by temperature, lag 0–1 day, in Wuhan, China, July 2001–June 2004.

| Cause of death, pollutant | Temperature | | |
|---|---|---|---|
| | Normal | Low | High |
| Nonaccidental | | | |
| $PM_{10}$ | 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) |

The estimated $PM_{10}$ effects were attenuated in the two pollutant models (Table 6). For example, inclusion of $NO_2$ in the model substantially reduced the $PM_{10}$ effect for nonaccidental mortality at normal temperature, whereas the inclusion of $SO_2$ had less influence. These relationships were also present at low temperatures. Conversely, at high temperatures, the inclusion of either $NO_2$ or $SO_2$ had little influence on the association of $PM_{10}$ with nonaccidental mortality. Although $PM_{10}$ was correlated with both $NO_2$ and $SO_2$ (Table 7), the attenuation of the estimated effects in two-pollutant models might not be due simply to confounding, but rather an indicator of the source-related component of PM responsible for the adverse health effect. The sources and composition of $PM_{10}$, and hence the toxicity, vary with temperature. Thus, temperature may be serving as an indicator of $PM_{10}$ composition. The interaction of $O_3$ on nonaccidental mortality was attenuated but remained significant after controlling for $PM_{10}$ and $SO_2$ in the copollutant models (Table 8). Because temperature was positively correlated with $O_3$ ($r$ = 0.52), part of the interaction between $PM_{10}$ and high temperature might be due to $O_3$.

## Discussion and Conclusion

We observed that high temperatures enhanced $PM_{10}$ mortality effects, even though $PM_{10}$ daily concentrations were lower on the extremely high-temperature days than on the normal-temperature and low-temperature days.

The small number of previous relevant studies reported conflicting results on this interaction. Samet et al. (1998) found no significant evidence that weather variables modified the pollution–mortality relationship. However, Katsouyanni et al. (1993) found a significant effect of the interaction between $SO_2$ and high temperature on total mortality but no significant interactions between high temperature and either smoke or $O_3$. We speculate that the following environmental features are related to the significant synergistic effects of $PM_{10}$ and high temperature in Wuhan. First, the maximum summer temperature often exceeded 40°C and lasted about 2 weeks. Wuhan's special topography causes narrow differences in daily high and low temperatures. Even around midnight in

the summer, indoor air temperatures > 32°C are not uncommon. Thus, the city residents were exposed to high temperatures for longer periods than residents of many other cities. Second, few residences in Wuhan were built with energy conservation in mind; a vast amount of radiant energy can easily infiltrate buildings and be absorbed, even when all windows are closed. The temperature inside is 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 commonly used means for cooling are fans, which can be effective in protecting against heat stress in areas without extremely high temperatures. However, with the temperatures in Wuhan, the use of fans could contribute to heat stress by exacerbating dehydration (Centers for Disease Control and Prevention 1995). Finally, approximately 4.5 million permanent residents plus approximately 1 million transients live in the urban core districts with an area of 201 $km^2$. This high population density adds to the urban "heat island" effect, which would make the temperature somewhat higher in the urban core areas than in the suburban areas.

The mechanism underlying the synergistic effects of ambient particle pollution and extremely high temperatures on daily mortality is not yet clear. Some potential explanations have been proposed, especially for the elderly (Easterling et al. 2000). Brunekreef and Holgate (2002) hypothesized that air particles increase the risk of cardiopulmonary mortality through direct and indirect pathophysiologic mechanisms, including pulmonary and systemic inflammation, accelerated atherosclerosis, altered cardiac autonomic function, and increase of inflammatory cytokines in the heart. Many studies have addressed the mechanisms by which high temperature is associated with increased mortality. In animal studies, Keatinge et al. (1986) observed dehydration, increased intracranial and arterial hypertension, endothelial cell damage, and cerebral ischemia during the onset of heat stroke in animals exposed to high temperatures. In a clinical trial study, Gordon et al. (1988) found that exposure to high temperatures increased plasma viscosity and serum cholesterol level. Tsai et al. (2003) suggested that high temperature may help precipitate coronary artery disease and cerebral infarction. Flynn et al. (2005) observed that many of the elderly who died in the heat wave in France during the first 2 weeks of August 2003 were dehydrated, hypernatremic, and hyperkalemic, with evidence of renal failure (Vanhems et al. 2003). The investigators postulated that the most probable causes of death during the heat wave were thromboembolic disease and malignant cardiac arrhythmias as well as heat-induced sepsislike shock (Flynn et al. 2005).

Our study has several limitations. First, both ICD-9 and ICD-10 codes were used. The change in ICD coding might produce misclassification in cause-specific mortality. To address this uncertainty, we examined daily death counts between ICD-9 and ICD-10 mortality data in 2002. We found high concordance rates between the two-coded mortality data, and the maximum change in the estimated pollution mortality effect was 0.09%. These results support our contention that the change in the ICD coding system did not significantly affect the associations identified in this study. Second, there might be other important unknown and unmeasured factors. For example, socioeconomic status can play an important role as an effect modifier. Unfortunately, we do not currently have data on hand to explore the effects of these factors. Third, interpretation of the effects of interaction between $O_3$ and temperature requires caution, because $O_3$ data were obtained from only one monitoring station. The limited $O_3$ data may also restrict our ability to reach any reliable conclusion. Last, measurement errors in exposure are clearly applicable to this study. However, this measurement error generally belongs to the Berkson type and thus is nondifferential in nature, which is likely to cause a bias toward the null and lead to underestimated associations (Armstrong 1998).

In conclusion, we found synergistic effects between $PM_{10}$ and extremely high temperature on daily mortality in this highly polluted city. Further studies are needed to confirm these findings.

**Table 7.** Pearson correlations between daily measurements of pollutants in Wuhan, China, stratified by temperature, July 2001–June 2004.

| Temperature, pollutant | $NO_2$ | $SO_2$ | $O_3$ |
|---|---|---|---|
| Normal | | | |
| $PM_{10}$ | 0.72 | 0.59 | 0.06 |
| $NO_2$ | | 0.75 | 0.04 |
| $SO_2$ | | | 0.01 |
| Low | | | |
| $PM_{10}$ | 0.83 | 0.74 | 0.19 |
| $NO_2$ | | 0.87 | 0.31 |
| $SO_2$ | | | 0.33 |
| High | | | |
| $PM_{10}$ | 0.68 | 0.15 | 0.65 |
| $NO_2$ | | 0.45 | 0.65 |
| $SO_2$ | | | 0.42 |

**Table 8.** Copollutant regression estimates of the mean percentage of change (95% CI) in daily mortality per 10-μg/$m^3$ increase in $O_3$ concentrations by temperature, lag 0–1 day mean, in Wuhan, China, July 2001–June 2004.

| Cause of death, pollutant | Temperature | | |
|---|---|---|---|
| | Normal | Low | High |
| Nonaccidental | | | |
| $O_3$ | 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) |
| Noncardiopulmonary | | | |
| $O_3$ | 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) |

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# The Public Health and Air Pollution in Asia (PAPA) Project: Estimating the Mortality Effects of Particulate Matter in Bangkok, Thailand

*Nuntavarn Vichit-Vadakan,[1] Nitaya Vajanapoom,[1] and Bart Ostro[2]*

[1]Faculty of Public Health, Thammasat University, Rangsit Campus, Klongluang, Pathumthani, Thailand; [2]Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Oakland, California, USA

**Background:** Air pollution data in Bangkok, Thailand, indicate that levels of particulate matter with aerodynamic diameter ≤ 10 μm ($PM_{10}$) are significantly higher than in most cities in North America and Western Europe, where the health effects of $PM_{10}$ are well documented. However, the pollution mix, seasonality, and demographics are different from those in developed Western countries. It is important, therefore, to determine whether the large metropolitan area of Bangkok is subject to similar effects of $PM_{10}$.

**Objectives:** This study was designed to investigate the mortality risk from air pollution in Bangkok, Thailand.

**Methods:** The study period extended from 1999 to 2003, for which the Ministry of Public Health provided the mortality data. Measures of air pollution were derived from air monitoring stations, and information on temperature and relative humidity was obtained from the weather station in central Bangkok. The statistical analysis followed the common protocol for the multicity PAPA (Public Health and Air Pollution Project in Asia) project in using a natural cubic spline model with smooths of time and weather.

**Results:** The excess risk for non-accidental mortality was 1.3% [95% confidence interval (CI), 0.8–1.7] per 10 μg/m$^3$ of $PM_{10}$, with higher excess risks for cardiovascular and above age 65 mortality of 1.9% (95% CI, 0.8–3.0) and 1.5% (95% CI, 0.9–2.1), respectively. In addition, the effects from $PM_{10}$ appear to be consistent in multipollutant models.

**Conclusions:** The results suggest strong associations between several different mortality outcomes and $PM_{10}$. In many cases, the effect estimates were higher than those typically reported in Western industrialized nations.

**Key words:** air pollution, Bangkok, mortality, $PM_{10}$, time series. *Environ Health Perspect* 116:1179–1182 (2008). doi:10.1289/ehp.10849 available via *http://dx.doi.org/* [Online 9 July 2008]

Compelling epidemiologic evidence indicates that current ambient levels of airborne particulate matter (PM) in North American and Western European (NAWE) cities are associated with premature mortality and a wide range of morbidity outcomes [U.S. Environmental Protection Agency (EPA) 2004; World Health Organization (WHO) 2000]. Existing air pollution monitoring information and recent exposure assessments suggest that 6 to 10 million residents of Bangkok, Thailand, are exposed to levels of particulate matter with aerodynamic diameter ≤ 10 μm ($PM_{10}$) that are as high as or higher than those in NAWE cities. A recent review of Asian cities, mostly in more developed countries, suggests that PM may also be associated with both mortality and morbidity [Health Effects Institute (HEI) 2004]. However, PM chemical composition and relevant population characteristics, such as activity patterns, background health status, and other factors related to socioeconomic status, may all contribute to differential risks in developing countries such as Thailand. In addition, studies of mortality and air pollution in cities like Bangkok, which have seasonal patterns dramatically different from those of NAWE, provide an opportunity to assess the potentially confounding aspects of seasonality. Bangkok's climate is hot and humid throughout the year, with 24-hr average temperatures almost always above 80°F. Therefore, with the lack of a cold season, the seasonal weather patterns are very different from those observed in most previous studies.

The question remains whether residents of cities in developing countries are adversely affected by the existing levels of $PM_{10}$ and whether the impacts per unit are similar to those experienced in developed Western countries. Improvements in the mortality data collection system and air monitoring program in Bangkok provide an excellent opportunity to examine the effects of $PM_{10}$ and several gaseous pollutants on daily mortality for the years 1997 through 2003.

## Methods

*Data.* Our study period extended from 1999 through 2003. We obtained daily mortality data from the Ministry of Public Health, which currently uses the *International Classification of Diseases, 10th Revision* (ICD-10) to categorize cause of death (WHO 1992). For all ages, we abstracted those with "non-accidental" mortality (i.e., total mortality minus accidents and homicides), respiratory-specific mortality, cardiovascular-specific mortality, and mortality for some additional subcategories including ischemic heart disease, stroke, conduction disorders, respiratory mortality for those < 1 year of age, lower respiratory infection (LRI) for those < 5 years of age, chronic obstructive pulmonary disease (COPD), asthma, and senility. The latter was included as an end point because our preliminary analysis showed a relatively low number of daily deaths from cardiovascular diseases and a high number from senility. We speculated that the high apparent mortality from senility might have been the result of mislabeling the cause of death from cardiovascular diseases to senility, especially among the elderly dying outside the hospitals. We also classified nonaccidental mortality by various age groups and by sex.

In Bangkok, five ambient and seven roadside monitoring stations have been measuring hourly ambient levels of $PM_{10}$ since 1996; ten stations measure hourly ambient nitrogen dioxide, sulfure dioxide, and nitric oxide; and eight stations measure hourly ambient ozone. Because of road traffic congestion, we used $PM_{10}$ data from the five ambient monitoring stations to represent general population exposure. Based on the common protocol, days with < 18 hourly readings were considered missing. We calculated 24-hr averages for $NO_2$, NO (using the difference between $NO_x$ and $NO_2$), $SO_2$, and $PM_{10}$, with the requirement that at least 75% of 1-hr values be available on that particular day. For the 8-hr average value of $O_3$, at least six hourly values from 0100 to 1800 hours had to be available, because the maximum $O_3$ levels always occur during daylight. We calculated the daily concentrations for each pollutant in the analysis

Address correspondence to N. Vajanapoom, Faculty of Public Health, Thammasat University, Rangsit Campus, Klongluang, Pathumthani 12121, Thailand. Telephone: 662-516-7614. Fax: 662-516-7614. E-mail: nvajanapoom@yahoo.com

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by taking the mean of all available monitoring stations. We used only the stations that provided at least 75% completeness of the measurements over the study period.

Daily weather data are available at two locations (the airport and city center) and are highly correlated (Ostro et al. 1999). Therefore, we used data from the metropolitan weather station in the center of Bangkok, because there were no missing values. The data obtained included average daily temperature and average daily relative humidity.

***Statistical approach.*** To assess the short-term effects of $PM_{10}$ on daily mortality, we followed a common protocol developed by participants in the Public Health and Air Pollution Project in Asia (PAPA project), which included research teams representing Bangkok and Hong Kong, Shanghai, and Wuhan, China. We used Poisson regression, conditional on several independent variables, to control for temporal trends and meteorologic conditions. For the basic model, we used natural cubic spline models with smoothing for time and weather, using R software (version 2.5 with mgcv 1.3–24; R Development Core Team 2007). The natural spline model is a parametric approach that fits cubic functions joined at knots, which are typically placed evenly throughout the distribution of the variable of concern, such as time. The number of knots determines the overall smoothness of the fit. We determined the "best" core model for all nonaccidental cause mortality, controlling for time trend, seasonality, temperature, relative humidity, day of week, and public holidays, before entering an air pollutant into the model. In developing the core model, all PAPA cities examined 4–6 degrees of freedom (df) per year for the smoothing of time trend and 3 df for the smoothing of same-day lag of daily mean temperature and daily mean relative humidity. Preliminary analysis indicated that models with 4 or 5 df for time had mild autocorrelation, which would bias the standard errors. In contrast, a model with 6 df for the smoothing of time and first- and second-order autocorrelation terms resulted in no remaining serial correlation. Therefore, all subsequent models used this specification, although the results were very similar to those derived from the model unadjusted for autocorrelation. Based on the agreed-upon PAPA protocol, our core model used a lag of zero and 1 day (lag01) (i.e., the average of current day's and previous day's values), but single-day lags up to 5 days and moving averages of up to 5 days were also examined.

We conducted several sensitivity analyses to assess the impacts of different model specifications in our results. This included models with *a*) different lags of $PM_{10}$, *b*) various sets of degrees of freedom for time and weather, *c*) different lags of temperature and relative humidity, and *d*) penalized splines for time and weather in place of natural splines. We also fitted co-pollutant models assessing the effects of $PM_{10}$ with adjustment for gaseous pollutants. An influenza epidemic could be a potential confounder of the associations, a possibility we assessed in the sensitivity analysis. Unfortunately, daily death counts for influenza in Bangkok were likely to be underreported, so we defined influenza epidemic according to whether the weekly respiratory mortality count was greater than the 90th percentile of each year.

All results are presented in terms of the excess risk (ER) per 10 μg/m$^3$ of $PM_{10}$, which was calculated from the relative risk (RR) as ER = (RR –1) × 100.

**Table 1.** Average daily mortality in Bangkok, 1 January 1999 to 31 December 2003.

| Mortality | ICD-10 codes | Deaths/day ± SD |
|---|---|---|
| Nonaccidental | A00–R99 | 95.0 ± 12.1 |
| (age, years) | | |
| < 5 | | 3.0 ± 1.8 |
| 4–44 | | 29.0 ± 5.9 |
| 18–50 | | 34.0 ± 6.4 |
| 45–64 | | 27.0 ± 5.4 |
| > 50 | | 66.0 ± 9.9 |
| ≥ 65 | | 45.0 ± 7.9 |
| ≥ 75 | | 21.0 ± 5.2 |
| Male | | 61.0 ± 8.9 |
| Female | | 43.0 ± 7.6 |
| Cardiovascular | I00–I99 | 13.0 ± 4.3 |
| Ischemic heart diseases | I20–I25 | 4.0 ± 2.3 |
| Stroke | I60–I69 | 5.0 ± 2.5 |
| Conduction disorder | I44–I49 | 1.0 ± 0.5 |
| Cardiovascular ≥ age 65 | I00–I99 | 6.7 ± 3.0 |
| Respiratory | J00–J98 | 8.0 ± 3.1 |
| Respiratory < age 1 | J00–J98 | 0.1 ± 0.4 |
| LRI < 5 years | J10–J22 | 1.0 ± 0.4 |
| COPD | J40–J47 | 2.0 ± 1.0 |
| Asthma | J45–J46 | 1.2 ± 0.4 |
| Respiratory > age 65 | J00–J98 | 3.5 ± 2.0 |
| Senility | R54 | 14.0 ± 4.2 |

## Results

***Descriptive analysis.*** Table 1 summarizes the daily mortality data in Bangkok from 1 January 1999 to 31 December 2003. There was an average of 95 deaths per day from nonaccidental mortality. About 8% and 14% of the total consisted of mortality from respiratory and cardiovascular diseases, respectively, and about half of the total deaths were among those ≥ 65 years of age. Males make up about 64% of the total mortality in Bangkok. This may be attributable simply to the higher numbers of males in the city, possibly because of employment opportunities. We observed slightly increasing trends without apparent seasonal patterns in mortality data for Bangkok, suggesting that trend and seasonality may not be the strong confounding factors for the acute effects of $PM_{10}$ on mortality.

Table 2 provides the statistical distributions of the air pollutants and weather data used in this analysis, which were 100% complete over the study period except for $PM_{10}$, which had 4 missing days. Mean $PM_{10}$ was 52 μg/m$^3$, with a maximum value of 169.2 μg/m$^3$, higher than in most cities in NAWE. We observed a high correlation between $PM_{10}$ and both $NO_2$ ($r$ = 0.78) and $O_3$ ($r$ = 0.59). The weather in Bangkok was generally hot and humid. The median 24-hr temperature was 29.9°C and the median daily average humidity was 73.1%.

***Analytical results.*** Table 3 summarizes the results of pollutant models per 10-μg/m$^3$ increase in $PM_{10}$ for various disease-specific causes of mortality as well as age- and sex-specific mortality using lag01. We observed statistically significant associations with most of the outcomes including nonaccidental and cardiovascular mortality, and we observed a positive but nonsignificant association for this lag for respiratory mortality. The ER for nonaccidental mortality was 1.3% [95% confidence interval (CI), 0.8–1.7] for a 10-μg/m$^3$ increase in $PM_{10}$, with ER for cardiovascular and respiratory mortality of 1.9% (95% CI, 0.8–3.0) and 1.0% (95% CI, –0.4 to 2.4), respectively. With respect to subclassifications of cardiovascular disease, many were associated with $PM_{10}$, with mortality from stroke demonstrating a particularly elevated risk. Among the subgroups of respiratory mortality, we observed elevated excess risks for young children, especially among infants with respiratory causes, and asthma. Some of these estimates had very wide CIs, likely due to the small number of mortality counts for these outcomes. As indicated above, we also examined death from senility and found an excess

**Table 2.** Distribution of air pollutants and meteorology data in Bangkok, 1 January 1999 to 31 December 2003.

| Pollutants and meteorology | Mean | Min | Max | SD | Percentiles 5th | 25th | 50th | 75th | 95th | No. of days |
|---|---|---|---|---|---|---|---|---|---|---|
| $PM_{10}$ (μg/m$^3$) | 52.1 | 21.3 | 169.2 | 20.1 | 29.6 | 38.9 | 46.8 | 59.9 | 93.2 | 1,822 |
| $SO_2$ (μg/m$^3$) | 13.2 | 1.5 | 61.2 | 4.8 | 7.1 | 10.1 | 12.5 | 15.6 | 21.0 | 1,826 |
| $NO_2$ (μg/m$^3$) | 44.7 | 15.8 | 139.6 | 17.3 | 24.4 | 31.7 | 39.7 | 54.8 | 79.3 | 1,826 |
| $O_3$ (μg/m$^3$) | 59.4 | 8.2 | 180.6 | 26.4 | 25.3 | 39.1 | 59.4 | 75.3 | 109.8 | 1,826 |
| NO (μg/m$^3$) | 28.0 | 3.7 | 126.9 | 14.2 | 11.4 | 18.1 | 28.0 | 34.9 | 56.0 | 1,826 |
| Temperature (°C) | 28.9 | 18.7 | 33.6 | 1.7 | 25.8 | 28.1 | 29.1 | 29.9 | 31.3 | 1,826 |
| Relative humidity (%) | 72.8 | 41.0 | 95.0 | 8.3 | 58.0 | 67.8 | 73.1 | 78.3 | 86.0 | 1,826 |

Max, maximum; Min, minimum.

risk of 1.8% (95% CI, 0.7–2.8) which was similar to that of cardiovascular at ≥ 65 years of age.

Analysis of nonaccidental mortality by age group indicated that the effects of $PM_{10}$ increased with age, with the strongest effects for ages ≥ 75 years. However, associations were observed for all of the other age groups and, as indicated above, for respiratory mortality for children < 1 year of age. Our analysis by sex demonstrated relatively similar effects for males and females.

Table 4 summarizes the effects of different lags of $PM_{10}$ on several mortality outcomes. For nonaccidental and ≥ 65 mortality, of the single-day lags, unlagged $PM_{10}$ provided the highest ER. For cardiovascular and respiratory mortality, the highest ER was observed for single-day lags of 1 and 3 days, respectively. However, for all end points, cumulative averages of 5 days of pollution generated the highest risk estimates.

Table 5 summarizes the results of the sensitivity analysis, with a focus on all-cause and cardiovascular mortality. The table indicates the effects on the ER for different df in the smoothing of time, and for multipollutant models. We examined models with 3 to 15 df per year for time, and the results were generally insensitive to the number of df specified. In addition, the inclusion of $SO_2$, $NO_2$, or $O_3$ in the model had either no effect or slightly attenuated the estimated effect of $PM_{10}$. Finally, the results were generally insensitive to different lags and df for smoothing for temperature and humidity (however, overall, a lag0 temperature and humidity smooth term provided the best model fit, based on the percent of the explained deviation), use of penalized spline models, and inclusion of a term for influenza epidemics. In addition, the results for senility and for cardiovascular together with senility were similar and generally insensitive to the model specifications indicated above.

## Discussion

The results of our analysis of 5 years of data from Bangkok, Thailand, indicate a statistically significant association between daily mortality and daily concentrations of $PM_{10}$. For $PM_{10}$, the effect estimates for nonaccidental, cardiovascular, respiratory, and age ≥ 65 (nonaccidental) mortality are generally similar to (but in the high range) of those found elsewhere (U.S. EPA 2004). A 10-μg/m$^3$ increase in lag01 $PM_{10}$ was associated with an excess risk in nonaccidental, cardiovascular, respiratory, and age ≥ 65 mortality of 1.3, 1.9, 1.0, and 1.5%, respectively. These estimates are generally similar to those reported by Ostro et al. (1998, 1999) and Vajanapoom et al. (2002) in studies of Bangkok covering earlier years. However, these studies largely used $PM_{10}$ data estimated from airport visibility rather than the direct measurements of $PM_{10}$ used here.

Excess risks from $PM_{10}$ were observed for many of the cardiovascular- and respiratory-disease specific subclasses of mortality, with particularly high risks related to respiratory diseases for those < 1 year of age, asthma, LRI, stroke, and senility. The similar magnitudes of the excess risks on cardiovascular age ≥ 65 years and senility suggested that the latter probably includes cardiovascular mortality that has been incorrectly classified, especially for the elderly dying outside of hospitals, where the cause of death is often diagnosed as senility by a nonphysician coroner. Analysis by age indicated associations with $PM_{10}$ for all of the subgroups, and our examination of lags indicated that multiday averages of 5 days generated the largest effect estimates. In addition, many of the $PM_{10}$ associations were retained in multipollutant models. The results of the sensitivity analyses indicate that our core model was generally robust to choices of model specifications, spline model used, degrees of freedom of time smoothers, lags for temperature, adjustment for autocorrelation, and adjustment for influenza epidemics.

Generally our analysis of $PM_{10}$ per 10 μg/m$^3$ in Bangkok generated effect estimates that are higher than most previously reported. For example, our estimate for nonaccidental mortality is 1.3% (95% CI, 0.8–1.7%). In comparison, an analysis of 75 single-city time-series analyses from around the world generated an estimate of 0.6% (95% CI, 0.5–0.7%) (Anderson et al. 2005). A study of the 90 largest cities in the United States gave an estimate of 0.2% (95% CI, 0.1–0.4%) (Dominici et al. 2003), whereas a study of 29 European cities yielded an estimate of 0.6% (95% CI, 0.4–0.7%) (Katsouyanni et al. 2003). A study of 14 cities in the United States using a case–crossover approach generated an estimate of 0.35% (95% CI, 0.2–0.5%) (Schwartz 2004). A meta-analysis of Asian studies using a random-effects estimate gave an estimate of 0.49% (95% CI, 0.23–0.76%) based on four cities: Bangkok; Seoul and Inchon, South Korea; and Hong Kong (HEI 2004). Thus, it is clear that the results for Bangkok are at the upper end of the range of estimates. It is also significant that some high estimates have been reported in other less-developed countries. For example, a study in Mexico City reported an

**Table 3.** Percent ER in mortality (95% CI) for a 10-μg/m$^3$ increase in lag01 $PM_{10}$.[a]

| Mortality | %ER (95% CI) |
|---|---|
| Cause-specific | |
| Nonaccidental | 1.3 (0.8 to 1.7) |
| Cardiovascular | 1.9 (0.8 to 3.0) |
| Ischemic heart disease | 1.5 (–0.4 to 3.5) |
| Stroke | 2.3 (0.6 to 4.0) |
| Conduction disorders | –0.3 (–5.9 to 5.6) |
| Cardiovascular ≥ age 65 | 1.8 (0.2 to 3.3) |
| Respiratory | 1.0 (–0.4 to 2.4) |
| Respiratory ≤ age 1 | 14.6 (2.9 to 27.6) |
| LRI < age 5 | 7.7 (–3.6 to 20.3) |
| COPD | 1.3 (–1.8 to 4.4) |
| Asthma | 7.4 (1.1 to 14.1) |
| Respiratory ≥ age 65 | 1.3 (–0.8 to 3.3) |
| Senility | 1.8 (0.7 to 2.8) |
| Age-specific for nonaccidental (years) | |
| 0–4 | 0.2 (–2.0 to 2.4) |
| 5–44 | 0.9 (0.2 to 1.7) |
| 18–50 | 1.2 (0.5 to 1.9) |
| 45–64 | 1.1 (0.4 to 1.9) |
| ≥ 50 | 1.4 (0.9 to 1.9) |
| ≥ 65 | 1.5 (0.9 to 2.1) |
| ≥ 75 | 2.2 (1.3 to 3.0) |
| Sex-specific for nonaccidental | |
| Male | 1.2 (0.7 to 1.7) |
| Female | 1.3 (0.7 to 1.9) |

[a]Model covariates include smooth of time with 6 df, smooth of unlagged temperature and humidity with 3 df, and day of week.

**Table 5.** Percent ER (95% CI) in mortality for a 10-μg/m$^3$ increase in $PM_{10}$ with alternative degrees of freedom for smoothing of time and with adjustment for gaseous pollutants.

| Model specification | %ER (95% CI) |
|---|---|
| Nonaccidental (df) | |
| 3 | 1.3 (0.9 to 1.8) |
| 4 | 1.2 (0.8 to 1.7) |
| 6 | 1.3 (0.8 to 1.7) |
| 6, with $SO_2$ | 1.2 (0.8 to 1.7) |
| 6, with $NO_2$ | 1.0 (0.2 to 1.8) |
| 6, with $O_3$ | 1.1 (0.6 to 1.7) |
| 9 | 1.1 (0.7 to 1.6) |
| 12 | 1.1 (0.6 to 1.5) |
| 15 | 1.2 (0.7 to 1.6) |
| Cardiovascular (df) | |
| 3 | 1.8 (0.8 to 2.7) |
| 4 | 1.6 (0.7 to 2.6) |
| 6 | 1.7 (0.7 to 2.7) |
| 6, with $SO_2$ | 2.0 (0.9 to 3.3) |
| 6, with $NO_2$ | 2.3 (0.2 to 4.3) |
| 6, with $O_3$ | 1.8 (0.5 to 3.2) |
| 9 | 1.7 (0.6 to 2.8) |
| 12 | 1.8 (0.7 to 3.0) |
| 15 | 2.2 (0.9 to 3.4) |

**Table 4.** Lag effects of $PM_{10}$ for major causes of mortality [percent ER (95% CI)].

| Lag days | Nonaccidental | Cardiovascular | Respiratory | Age ≥ 65 |
|---|---|---|---|---|
| Lag0 | 1.2 (0.8 to 1.6) | 1.5 (0.5 to 2.6) | 1.0 (–0.3 to 2.3) | 1.5 (0.9 to 2.0) |
| Lag1 | 0.9 (0.6 to 1.3) | 1.7 (0.7 to 2.7) | 0.8 (–0.5 to 2.0) | 1.1 (0.6 to 1.7) |
| Lag2 | 0.9 (0.5 to 1.3) | 1.6 (0.6 to 2.6) | 1.1 (–0.1 to 2.3) | 1.1 (0.6 to 1.6) |
| Lag3 | 0.8 (0.4 to 1.2) | 0.8 (–0.1 to 1.8) | 1.3 (0.1 to 2.6) | 1.2 (0.6 to 1.7) |
| Lag4 | 0.3 (–0.1 to 0.7) | –0.1 (–1.1 to 0.9) | 0.7 (–0.6 to 1.9) | 0.7 (0.2 to 1.2) |
| 0–1 mean | 1.3 (0.8 to 1.7) | 1.9 (0.8 to 3.0) | 1.0 (–0.4 to 2.4) | 1.5 (0.9 to 2.1) |
| 0–4 mean | 1.4 (0.9 to 1.9) | 1.9 (0.6 to 3.2) | 1.9 (1.2 to 2.6) | 1.9 (1.2 to 2.6) |

excess risk of 1.8% (95% CI, 0.9–2.7%), whereas analysis of Santiago, Chile, found an excess risk of 1.1% (95% CI, 0.9–1.4%) (Castillejos et al. 2000; Ostro et al. 1996).

We can speculate on several possible reasons for our findings, including *a*) differences in particle chemistry in Bangkok; *b*) the proximity of a large proportion of the population to roads and traffic congestion; *c*) the likely high penetration rates due to low prevalence of home air conditioning in favor of open ventilation between indoors and outdoors (Tsai et al. 2000); *d*) the greater duration of exposure due to the amount of time spent outdoors, because many Thais work and eat outdoors; *e*) factors related to lower economic development and socioeconomic status, such as lower background health status and use of health care, and higher smoking rates and co-morbidity; *f*) greater exposure to indoor sources such as incense and cooking; and *g*) stochastic variability. Because of several of these factors (although only anecdotal in nature), it is likely that the effective inhaled dose of any given concentration measured from a fixed site outdoor monitor is greater in Bangkok than in Western industrialized countries.

To date, few studies that relate mortality to air pollution have been conducted in Asia. Studies of daily mortality have been conducted in Inchon (Hong et al. 1999), Seoul, and Ulsan, South Korea (Kwon et al. 2001; Lee and Schwartz 1999; Lee et al. 1999); Shenyang, China (Xu et al. 2000); seven cities in South Korea (Lee et al. 2000); and New Delhi, India (Cropper et al. 1997). For the most part, policy makers in Asia have had to draw from studies conducted in North America and Western Europe. Although it may be reasonable to extrapolate the findings from the NAWE region to other parts of the world, our study also suggests that the per-unit effects may be higher in certain developing countries. Additional studies undertaken in developing countries in Asia and other parts of the world can validate our findings and help determine the factors that might modify the effect estimate.

Finally, our analysis demonstrated an association between air pollution and mortality in a region that would not be confounded by cold weather and associated respiratory infections. As such, it supports the likelihood of a causal association in studies in NAWE, which experience greater seasonality and colder temperatures.

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# Season, Sex, Age, and Education as Modifiers of the Effects of Outdoor Air Pollution on Daily Mortality in Shanghai, China: The Public Health and Air Pollution in Asia (PAPA) Study

*Haidong Kan,[1,2] Stephanie J. London,[2] Guohai Chen,[3] Yunhui Zhang,[1] Guixiang Song,[4] Naiqing Zhao,[5] Lili Jiang,[4] and Bingheng Chen[1]*

[1]Department of Environmental Health, School of Public Health, Fudan University, Shanghai, China; [2]Epidemiology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, U.S. Department of Health and Human Services, Research Triangle Park, North Carolina, USA; [3]Shanghai Environmental Monitoring Center, Shanghai, China; [4]Shanghai Municipal Center of Disease Control and Prevention, Shanghai, China; [5]Department of Health Statistics, School of Public Health, Fudan University, Shanghai, China

**Background:** Various factors can modify the health effects of outdoor air pollution. Prior findings about modifiers are inconsistent, and most of these studies were conducted in developed countries.

**Objectives:** We conducted a time-series analysis to examine the modifying effect of season, sex, age, and education on the association between outdoor air pollutants [particulate matter < 10 μm in aerodynamic diameter ($PM_{10}$), sulfur dioxide, nitrogen dioxide, and ozone] and daily mortality in Shanghai, China, using 4 years of daily data (2001–2004).

**Methods:** Using a natural spline model to analyze the data, we examined effects of air pollution for the warm season (April–September) and cool season (October–March) separately. For total mortality, we examined the association stratified by sex and age. Stratified analysis by educational attainment was conducted for total, cardiovascular, and respiratory mortality.

**Results:** Outdoor air pollution was associated with mortality from all causes and from cardiorespiratory diseases in Shanghai. An increase of 10 μg/m$^3$ in a 2-day average concentration of $PM_{10}$, $SO_2$, $NO_2$, and $O_3$ corresponds to increases in all-cause mortality of 0.25% [95% confidence interval (CI), 0.14–0.37), 0.95% (95% CI, 0.62–1.28), 0.97% (95% CI, 0.66–1.27), and 0.31% (95% CI, 0.04–0.58), respectively. The effects of air pollutants were more evident in the cool season than in the warm season, and females and the elderly were more vulnerable to outdoor air pollution. Effects of air pollution were generally greater in residents with low educational attainment (illiterate or primary school) compared with those with high educational attainment (middle school or above).

**Conclusions:** Season, sex, age, and education may modify the health effects of outdoor air pollution in Shanghai. These findings provide new information about the effects of modifiers on the relationship between daily mortality and air pollution in developing countries and may have implications for local environmental and social policies.

**Key words:** air pollution, modifiers, mortality, time-series studies. *Environ Health Perspect* 116:1183–1188 (2008). doi:10.1289/ehp.10851 available via *http://dx.doi.org/* [Online 9 July 2008]

Epidemiologic studies have reported associations of outdoor air pollution with daily mortality and morbidity from cardiorespiratory diseases (Goldberg et al. 2003). Multicity analyses conducted in the United States, Canada, and Europe provide further evidence supporting coherence and plausibility of the associations (Burnett et al. 2000; Dominici et al. 2006; Katsouyanni et al. 1997, 2001; Samet et al. 2000a). Recently, interest has been focused on the possible modifying effect of season (Peng et al. 2005; Touloumi et al. 2006; Zeka et al. 2006), preexisting health status (Bateson and Schwartz 2004; Goldberg et al. 2001; Katsouyanni et al. 2001), and population demographic characteristics such as sex and age (Atkinson et al. 2001; Bateson and Schwartz 2004; Cakmak et al. 2006; Katsouyanni et al. 2001) on the relation between air pollution and daily mortality. It is also hypothesized that the effects of air pollution exposure on health are greater in people with lower socioeconomic status (SES) (O'Neill et al. 2003). However, prior findings about the modifying effect of SES remain inconsistent: some studies found evidence of modification (Finkelstein et al. 2003; Jerrett et al. 2004; Krewski et al. 2005; Zeka et al. 2006), but others did not (Bateson and Schwartz 2004; Cakmak et al. 2006; Samet et al. 2000b; Zanobetti and Schwartz 2000). Moreover, most of these studies were conducted in developed countries, and only a small number of studies have been conducted in Asia (Health Effects Institute 2004). The need remains for studies of cities in developing countries, where characteristics of outdoor air pollution (e.g., air pollution level and mixture, transport of pollutants), meteorological conditions, and sociodemographic patterns may differ from those in North America and Europe.

Better knowledge of these modifying factors will help in public policy making, risk assessment, and standard setting, especially in cities of developing countries with fewer existing studies. In the present study, we conducted a time-series analysis to examine the modifying effect of season, sex, age, and education on the association between outdoor air pollutants [particulate matter < 10 μm in diameter ($PM_{10}$), sulfur dioxide, nitrogen dioxide, and ozone] and daily mortality in Shanghai, China. This study is a part of the joint Public Health and Air Pollution in Asia (PAPA) program supported by the Health Effects Institute (HEI).

## Materials and Methods

*Data.* Shanghai, the most populous city in China, comprises urban/suburban districts and counties, with a total area of 6,341 km$^2$ and had a population of 13.1 million by the end of 2004. Our study area was limited to the traditional nine urban districts of Shanghai (289 km$^2$). The target population includes all permanent residents living in the area—around 6.3 million in 2004. In the target population, the male/female ratio was 100.9%, and the elderly (> 65 years of age) accounted for 11.9% of the total population.

Daily nonaccidental mortality data from 1 January 2001 to 31 December 2004 were collected from the database of the Shanghai Municipal Center of Disease Control and Prevention (SMCDCP). Death certificates are completed either by community doctors for deaths at home or by hospital doctors for deaths in hospitals. The information on the certificates is then sent to the SMCDCP through their internal computer network. In Shanghai, all deaths must be reported to appropriate authorities before cremation. The database for 2001 and 2002–2004 was coded according to the *International Classification of Diseases, Revision 9* [ICD-9; World Health Organization (WHO) 1978] and *Revision 10*

Address correspondence to H. Kan, Department of Environmental Health, School of Public Health, Fudan University, Shanghai 200032, China. Telephone: 86 21 64046351. Fax: 86 21 64046351. E-mail: haidongkan@gmail.com

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(ICD-10; WHO 1993), respectively. The mortality data were classified into deaths due to all nonaccidental causes (ICD-9 codes < 800; ICD-10 codes A00–R99), cardiovascular diseases (ICD-9 codes 390–459; ICD-10 codes I00–I99), and respiratory diseases (ICD-9 codes 460–519; ICD-10 codes J00–J98). The data were also classified by sex and age (0–4, 5–44, 45–64, and ≥ 65 years) for all-cause deaths. Educational attainment has often been used as a surrogate indicator of SES in time-series studies (Cakmak et al. 2006; Jerrett et al. 2004; Zanobetti and Schwartz 2000; Zeka et al. 2006). We therefore classified all-cause, cardiovascular, and respiratory deaths by educational attainment (low, illiterate or primary school; high, middle school or above).

Daily air pollution data, including $PM_{10}$, $SO_2$, $NO_2$, and $O_3$, were retrieved from the database of the Shanghai Environmental Monitoring Center, the government agency in charge of collection of air pollution data in Shanghai. The daily concentrations for each pollutant were averaged from the available monitoring results of six fixed-site stations in the nine urban districts and covered by China National Quality Control. These stations are mandated to be located away from major roads, industrial sources, buildings, or residential sources of emissions from the burning of coal, waste, or oil; thus, our monitoring results reflect the background urban air pollution level in Shanghai rather than local sources such as traffic or industrial combustion.

We abstracted the daily 24-hr mean concentrations for $PM_{10}$, $SO_2$, and $NO_2$, and maximal 8-hr mean concentrations for $O_3$. The maximal 8-hr mean was used because the WHO (2000) recommended that the 8-hr mean reflects the most health-relevant exposure to $O_3$. For the calculation of both 24-hr mean concentrations of $PM_{10}$, $SO_2$, and $NO_2$, as well as maximal 8-hr mean $O_3$ concentrations, at least 75% of the 1-hr values must have been available on that particular day.

To allow adjustment for the effect of weather conditions on mortality, we obtained daily mean temperature and humidity data from the Shanghai Meteorological Bureau database. The weather data were measured at a single fixed-site station in the Xuhui District of Shanghai.

All of the mortality, weather, and air pollution data were validated by an independent auditing team assigned by the HEI. The team checked a sample of the original death certificates and monitoring records and validated the generation process of mortality, weather, and air pollution data used for the time-series analysis.

***Statistical methods.*** Our statistical analysis followed the Common Protocol of the PAPA program. We used a generalized linear model (GLM) with natural splines (ns) to analyze the data. First, we built the basic models for various mortality outcomes excluding the air pollution variables. We incorporated the ns functions of time and weather conditions, which can accommodate nonlinear and nonmonotonic relationships of mortality with time and weather variables, offering a flexible modeling tool (Hastie and Tibshirani 1990). We used the partial autocorrelation function (PACF) to guide the selection of degrees of freedom (df) for time trend (Katsouyanni et al. 2001; Touloumi et al. 2004, 2006). Specifically, we used 4–6 df per year for time trend. When the absolute magnitude of the PACF plot was < 0.1 for the first two lag days, the basic model was regarded as adequate; if this criterion was not met, autoregression terms for lag up to 7 days were introduced to improve the model. In this way, 4, 4, and 5 df per year for time trend, as well as 3, 2, and 4 lag-day autoregression terms, were used in our basic models for total, cardiovascular, and respiratory mortality, respectively. In addition, we used 3 df (whole period of study) for temperature and humidity because this has been shown to control well for their effects on mortality (Dominici et al. 2006; Samet et al. 2000a). Day of the week was included as a dummy variable in the basic models. We examined residuals of the basic models to determine whether there were discernable patterns and autocorrelation by means of residual plots and PACF plots. After we established the basic models, we introduced the pollutant variables and analyzed their effects on mortality outcomes.

Briefly, we fit the following log-linear GLM to obtain the estimated pollution log-relative rate β in Shanghai:

$$\begin{aligned} logE(Y_t) = \beta Z_t + DOW + ns(time, df) \\ + ns(temperature/humidity, 3) \\ + intercept, \end{aligned} \quad [1]$$

where $E(Y_t)$ represents the expected number of deaths at day $t$; β represents the log-relative rate of mortality associated with a unit increase of air pollutants; $Z_t$ indicates the pollutant concentrations at day $t$; $DOW$ is dummy variable for day of the week; $ns(time,df)$ is the ns function of calendar time; and $ns(temperature/humidity, 3)$ is the ns function for temperature and humidity with 3 df. Current-day temperature and humidity (lag 0) and 2-day moving average of air pollutant concentrations (lag 01) were used in our analyses.

We assessed both total nonaccidental and cause-specific mortality. We were able to stratify by sex and age only for total mortality. We analyzed effects of air pollution separately for the warm season (April–September) and the cool season (October–March) as well as for the entire year (Peng et al. 2005; Touloumi et al. 2006). The basic models of seasonal analyses were different from those of whole-period analyses, using various dfs for time trend. Analyses by educational attainment were conducted for total, cardiovascular, and respiratory mortality. We tested the statistical significance of differences between effect estimates of the strata of a potential effect modifier (e.g., the difference between females and males) by calculating the 95% confidence interval (CI) as

$$\left(\hat{Q}_1 - \hat{Q}_2\right) \pm 1.96\sqrt{\hat{SE}_1 + \hat{SE}_2}\,, \quad [2]$$

where $\hat{Q}_1$ and $\hat{Q}_2$ are the estimates for the two categories, and $\hat{SE}_1$ and $\hat{SE}_2$ are their respective SEs (Zeka et al. 2006). Regardless of significance, we considered modification of effect by a factor of ≥ 2 to be important and worthy of attention (Zeka et al. 2006).

As a sensitivity analysis, we also examined the impact of model specifications such as lag structure and df selection on the effects of air pollutants (Welty and Zeger 2005). We did not find substantial differences using alternative specifications.

All analyses were conducted in R, version 2.5.1, using the mgcv package (R Development Core Team 2007). The results are presented as the percent change in daily mortality per 10-μg/m$^3$ increase of air pollutants.

## Results

***Data description.*** From 2001 to 2004 (1,461 days), a total of 173,911 deaths (82,597 females and 91,314 males) were registered in the study population. The percentages of total deaths by age group were 0.3% for 0–4 years, 3.2% for 5–44 years, 13.0% for 45–64 years, and 83.5% for ≥ 65 years. On average, there were approximately 119 nonaccidental deaths per day, including 44 from cardiovascular diseases and 14 from respiratory diseases (Table 1). Cardiorespiratory disease accounted for 49.1% of total nonaccidental deaths.

During our study period, the mean daily average concentrations of $PM_{10}$, $SO_2$, $NO_2$, and $O_3$ were 102.0, 44.7, 66.6, and 63.4 μg/m$^3$, respectively. There were two missing value days for $O_3$ and none for the other three pollutants. The mean daily average temperature and humidity were 17.7°C and 72.9%, respectively, reflecting the subtropical climate in Shanghai.

Generally, $PM_{10}$, $SO_2$, and $NO_2$ were relatively highly correlated with each other (Pearson correlation coefficients ranged from 0.64 to 0.73). $PM_{10}$/$SO_2$/$NO_2$ concentrations were negatively correlated with temperature and humidity. Maximal 8-hr mean $O_3$ was weakly correlated with $PM_{10}$, $SO_2$, and $NO_2$ (Pearson correlation coefficients ranged from 0.01 to 0.19) and moderately correlated with temperature level (Pearson correlation coefficient, 0.48).

***Effects by season.*** In the whole-period analyses, outdoor air pollution was associated with mortality from all causes and from cardiopulmonary diseases in Shanghai (Table 2). An increase of 10 μg/m$^3$ of 2-day average concentrations of $PM_{10}$, $SO_2$, $NO_2$, and $O_3$ corresponds to 0.25% (95% CI, 0.14–0.37), 0.95% (95% CI, 0.62–1.28), 0.97% (95% CI, 0.66–1.27), and 0.31% (95% CI, 0.04–0.58) increase of all-cause mortality, respectively.

There were more deaths, higher concentrations of pollutants (except for $O_3$, which had higher concentrations in the warm season), and drier weather conditions in the cool season than in the warm season (Table 1).

The effect estimates of $PM_{10}$ on total mortality were similar in both seasons. Effect estimates were approximately 2–3 times higher for $SO_2$ and $NO_2$ in the cool season compared with the warm season. The effect estimate of $O_3$ was significant in both cool and warm seasons, and the magnitude of the $O_3$-associated increase in total mortality was approximately 5-fold higher in the cool season than in the warm season. Between-season differences in total mortality were significant for $NO_2$ and $O_3$ but not for $PM_{10}$ or $SO_2$ (Table 2).

For cardiovascular mortality, the effect estimate of $PM_{10}$ was similar in both seasons. For $SO_2$, $NO_2$, and $O_3$, the effect estimate in the cool season were approximately 3–4 times higher than in the warm season. Between-season differences in cardiovascular mortality were insignificant for all four pollutants.

For the smaller category of respiratory mortality, the effect estimates of $PM_{10}$, $SO_2$, and $NO_2$ were significant only in the cool season, and their between-season differences were significant. The effect effect estimate of $O_3$ on respiratory mortality was insignificant in either season.

***Effects by sex and age.*** The percent increase associated with higher concentration levels of air pollutants varied by sex or age group (Table 3). The effect estimates of $PM_{10}$ and $O_3$ among females were approximately twice those among males, although their between-sex differences were insignificant. The effect estimates of $SO_2$ and $NO_2$ on total mortality in females were slightly higher than in males.

The number of deaths for residents under 5 years of age was very low and therefore was excluded from our analysis. We did not observe significant effects of air pollution in residents 5–44 years of age or 45–64 years of age. Among those ≥ 65 years of age, the effect estimates of all four pollutants were significant, and approximately 2–5 times higher than among people 5–44 years of age or 45–64 years of age, although the between-age differences among all three groups were insignificant.

***Effects by education.*** Generally, residents with low educational attainment (illiterate or primary school) had a higher number of deaths from air pollution–related effects than those with high educational attainment (middle school or above) (Table 4).

For total mortality, the effect estimates of $PM_{10}$, $SO_2$, and $NO_2$ were significant in both education groups. The effect estimates of these three pollutants were 1–2 times larger among the low-education group compared with the high-education group, although the educational differences were significant only for $NO_2$ for total mortality. The effect estimate of $O_3$ of total mortality were similar and insignificant in both groups.

For cardiovascular mortality, the effect estimates of $PM_{10}$ and $NO_2$ were significant or marginally significant in both education groups; the effect estimate of $SO_2$ was significant only in the low-education group; no significant effect of $O_3$ was seen in either group. The effect estimates of all four pollutants were 1–2 times larger among the low-education group compared with the high-education group. The educational differences in cardiovascular mortality were not significant for any pollutants.

For respiratory mortality, the effect estimates of $PM_{10}$, $SO_2$, and $NO_2$ were significant only among those with low education, whereas the effect estimate of $O_3$ on respiratory mortality was not significant in either group. The effect estimates of $PM_{10}$, $SO_2$, and $NO_2$ were several times larger among the low-education group compared with the

**Table 1.** Daily deaths, air pollutant concentrations, and weather conditions (mean ± SE) in Shanghai, China, 2001–2004.

| | Warm season (*n* = 729) | Cool season (*n* = 732) | Entire period (*n* = 1,461) |
|---|---|---|---|
| No. of daily deaths | | | |
| Total (nonaccident) | 106.1 ± 0.5 | 132.0 ± 0.8 | 119.0 ± 0.6 |
| Cardiovascular | 37.9 ± 0.3 | 50.5 ± 0.4 | 44.2 ± 0.3 |
| Respiratory | 11.4 ± 0.1 | 17.2 ± 0.3 | 14.3 ± 0.2 |
| Air pollutant concentration (μg/m$^3$)[a] | | | |
| $PM_{10}$ | 87.4 ± 1.8 | 116.7 ± 2.8 | 102.0 ± 1.7 |
| $SO_2$ | 39.4 ± 0.7 | 50.1 ± 1.0 | 44.7 ± 0.6 |
| $NO_2$ | 57.3 ± 0.7 | 76.0 ± 1.0 | 66.6 ± 0.7 |
| $O_3$ | 78.4 ± 1.5 | 48.3 ± 0.9 | 63.3 ± 1.0 |
| Meteorological measures | | | |
| Temperature (°C) | 24.3 ± 0.2 | 11.2 ± 0.3 | 17.7 ± 0.2 |
| Humidity (%) | 75.1 ± 0.4 | 70.6 ± 0.5 | 72.9 ± 0.3 |

[a]Twenty-four-hour average for $PM_{10}$, $SO_2$, and $NO_2$; 8-hr (1000–1800 hours) average for $O_3$.

**Table 2.** Percent increase [mean (95% CI)] of mortality outcomes of Shanghai residents associated with 10-μg/m$^3$ increase in air pollutant concentrations by season, 2001–2004.[a]

| Mortality | Pollutant | Warm season | Cool season | Entire period |
|---|---|---|---|---|
| Total | $PM_{10}$ | 0.21 (0.09 to 0.33) | 0.26 (0.22 to 0.30) | 0.25 (0.14 to 0.37) |
| | $SO_2$ | 0.57 (–0.03 to 1.18) | 1.10 (0.66 to 1.53) | 0.95 (0.62 to 1.28) |
| | $NO_2$ | 0.46 (–0.07 to 0.98) | 1.24 (0.84 to 1.64)* | 0.97 (0.66 to 1.27) |
| | $O_3$ | 0.22 (0.03 to 0.41) | 1.19 (0.56 to 1.83)* | 0.31 (0.04 to 0.58) |
| Cardiovascular | $PM_{10}$ | 0.22 (–0.14 to 0.58) | 0.25 (0.05 to 0.45) | 0.27 (0.10 to 0.44) |
| | $SO_2$ | 0.31 (–0.65 to 1.29) | 1.02 (0.40 to 1.65) | 0.91 (0.42 to 1.41) |
| | $NO_2$ | 0.30 (–0.54 to 1.14) | 1.26 (0.68 to 1.84) | 1.01 (0.55 to 1.47) |
| | $O_3$ | 0.32 (–0.05 to 0.69) | 1.42 (0.51 to 2.33) | 0.38 (–0.03 to 0.80) |
| Respiratory | $PM_{10}$ | –0.28 (–0.93 to 0.38) | 0.58 (0.25 to 0.92)* | 0.27 (–0.01 to 0.56) |
| | $SO_2$ | –1.13 (–2.86 to 0.62) | 2.47 (1.41 to 3.54)* | 1.37 (0.51 to 2.23) |
| | $NO_2$ | –1.37 (–2.86 to 0.15) | 2.66 (1.67 to 3.65)* | 1.22 (0.42 to 2.01) |
| | $O_3$ | 0.12 (–0.72 to 0.98) | 0.94 (–0.60 to 2.50) | 0.29 (–0.44 to 1.03) |

[a]We used current day temperature and humidity (lag 0) and 2-day moving average of air pollutant concentrations (lag 01), and applied 3 df to temperature and humidity. *Significantly different from the warm season ($p < 0.05$).

**Table 3.** Percent increase [mean (95% CI)] in total mortality of Shanghai residents associated with a 10-μg/m$^3$ increase in air pollutant concentrations by sex and age.[a]

| | Mean daily deaths (*n*) | Pollutant | | | |
|---|---|---|---|---|---|
| | | $PM_{10}$ | $SO_2$ | $NO_2$ | $O_3$ |
| Sex | | | | | |
| Female | 56.5 | 0.33 (0.18 to 0.48) | 1.06 (0.62 to 1.51) | 1.10 (0.69 to 1.51) | 0.40 (0.03 to 0.76) |
| Male | 62.5 | 0.17 (0.03 to 0.32) | 0.85 (0.43 to 1.28) | 0.88 (0.49 to 1.28) | 0.19 (–0.16 to 0.55) |
| Age (years) | | | | | |
| 5–44 | 3.7 | 0.04 (–0.52 to 0.59) | 1.21 (–0.47 to 2.91) | 0.52 (–1.01 to 2.08) | –0.08 (–1.38 to 1.25) |
| 45–64 | 15.5 | 0.17 (–0.11 to 0.45) | 0.22 (–0.60 to 1.04) | 0.64 (–0.11 to 1.40) | 0.47 (–0.19 to 1.12) |
| ≥ 65 | 99.6 | 0.26 (0.15 to 0.38) | 1.01 (0.65 to 1.36) | 1.01 (0.69 to 1.34) | 0.32 (0.03 to 0.61) |

[a]We used current day temperature and humidity (lag 0) and 2-day moving average of air pollutant concentrations (lag 01), and applied 3 df to temperature and humidity.

high-education group. The educational differences in respiratory mortality were not significant for any pollutants.

## Discussion

Although the associations between outdoor air pollution and daily mortality have been well established in developed countries, the question of the potential modifiers remains inconclusive. As the U.S. National Research Council (1998) pointed out, it is important to understand the characteristics of individuals who are at increased risk of adverse events due to outdoor air pollution. Our results suggest that season and individual sociodemographic factors (e.g., sex, age, SES) may modify the health effects of air pollution in Shanghai. Specifically, the association between air pollution and daily mortality was generally more evident for the cool season than the warm season; females and the elderly (≥ 65 years of age) appeared to be more vulnerable to air pollution than males and younger people; and disadvantaged SES may intensify the adverse health effects of outdoor air pollution.

Our finding of a stronger association between air pollution and daily mortality in the cool season is consistent with several prior studies in Hong Kong (Wong et al. 1999, 2001) and Athens, Greece (Touloumi et al. 1996), but in contrast with others reporting greater effects in the warm season (Anderson et al. 1996; Bell et al. 2005; Nawrot et al. 2007). In Shanghai, the concentrations of $PM_{10}$, $SO_2$, and $NO_2$ were higher and more variable in the cool season than in the warm season (Table 1). Because these three pollutants were highly correlated, greater effects observed during the cool season may also be due to other pollutants that were also at higher levels during that season. In contrast, the $O_3$ level was higher in the warm season than in the cool season, and our exposure–response relationship also revealed a flatter slope at higher concentrations of $O_3$ for both sexes (data not shown). At higher concentrations, the risks of death could be reduced because vulnerable subjects may have died before the concentration reached the maximum level (Wong et al. 2001).

Exposure patterns may contribute to our season-specific observation. During the warm season, Shanghai residents tend to use air conditioning more frequently because of the relatively higher temperature and humidity, thus reducing their exposure. For example, in a survey of 1,106 families in Shanghai, 32.7% of the families never turn on air conditioners in the winter compared with 3.7% in the summer (Long et al. 2007). Heavy rain in the warm season may reduce time outdoors, thus reducing personal exposure. In contrast, the cool season in Shanghai is drier and less variable, so people are more likely to go outdoors and open the windows. Nevertheless, the fact that a consistently significant health effect of air pollution was observed only in the cool season in two subtropical Asian cities [Shanghai (present study) and Hong Kong (Wong et al. 1999, 2001)] suggests that the interaction of air pollution exposure and season may vary by location.

Unlike the gaseous pollutants, the constituents of the complex mix of $PM_{10}$ may vary by season. Therefore, another potential explanation for the seasonal difference in the effects of $PM_{10}$ is that the most toxic particles may have a cool-season maximum in Shanghai.

We found a greater effect of ambient air pollution on total mortality in females than in males. Results of prior studies on sex-specific acute effects of outdoor air pollution were discordant. For example, Ito and Thurston (1996) found the highest risk of mortality related with air pollution exposure among black women. Hong et al. (2002) found that elderly women were most susceptible to the adverse effects of $PM_{10}$ on the risk of acute mortality from stroke. However, Cakmak et al. (2006) found that sex did not modify the hospitalization risk of cardiac diseases due to air pollution exposure.

The reasons for our sex-specific observations are unclear and deserve further investigation. In Shanghai, females have a much lower smoking rate than males (0.6% in females vs. 50.6% in males) (Xu 2005). One study suggested that effects of air pollution may be stronger in nonsmokers than in smokers (Künzli et al. 2005). Oxidative and inflammatory effects of smoking may dominate to such an extent that the additional exposure to air pollutants may not further enhance effects along the same pathways in males. In addition, females have slightly greater airway reactivity than males, as well as smaller airways (Yunginger et al. 1992); therefore, dose–response relations might be detected more easily in females than in males. Deposition of particles in the lung varies by sex, with greater lung deposition fractions of 1-μM particles in all regions for females (Kim and Hu 1998; Kohlhaufl et al. 1999). Sunyer et al. (2000) suggested that differing particulate deposition patterns between females and males may partly explain the difference between the sexes. Moreover, compared with males, females in Shanghai had a lower education level (73.9% in females vs. 41.0% in males); thus, lower SES might contribute to the observed larger effects of air pollution in females.

As in a few other studies (Gouveia and Fletcher 2000; Katsouyanni et al. 2001), we found the elderly were most vulnerable to the effects of air pollution. Low numbers of deaths in the 0- to 4-year age group limited our power to detect the effects of air pollution on mortality, even if they exist. Two groups, the elderly and the very young, are presumed to be at greater risk for air pollution–related effects (Gouveia and Fletcher 2000; Schwartz 2004). For the elderly, preexisting respiratory or cardiovascular conditions are more prevalent than in younger age groups; thus, there is some overlap between potentially susceptible groups of older adults and people with heart or lung diseases.

It has long been known that SES can affect health indicators such as mortality (Mackenbach et al. 1997). Recently, studies have started to examine the role of SES in the vulnerability of subpopulations to outdoor air pollution, especially for particles and $O_3$, although the results remain inconsistent (O'Neill et al. 2003). For example, Zeka et al. (2006) found that individual-level education was inversely related to the risk of mortality associated with $PM_{10}$. Another cohort study with small-area measures of SES in Hamilton, Ontario, Canada, found important modification of the particle effects by social class (Finkelstein et al. 2003;

**Table 4.** Percent increase in number of deaths due to total, cardiovascular, and respiratory causes associated with a 10-μg/m$^3$ increase in air pollutants by educational attainment.[a]

| Mortality | Educational attainment | Mean daily deaths (*n*) | Pollutant | | | |
|---|---|---|---|---|---|---|
| | | | $PM_{10}$ | $SO_2$ | $NO_2$ | $O_3$ |
| Total | Low | 67.3 | 0.33 (0.19 to 0.47) | 1.19 (0.77 to 1.61) | 1.27* (0.89 to 1.66) | 0.26 (–0.09 to 0.60) |
| | High | 42.1 | 0.18 (0.01 to 0.36) | 0.66 (0.16 to 1.17) | 0.62 (0.15 to 1.09) | 0.30 (–0.11 to 0.71) |
| Cardiovascular | Low | 27.8 | 0.30 (0.10 to 0.51) | 1.08 (0.47 to 1.69) | 1.15 (0.58 to 1.72) | 0.39 (–0.13 to 0.90) |
| | High | 16.4 | 0.23 (–0.03 to 0.50) | 0.57 (–0.20 to 1.35) | 0.73 (0.01 to 1.45) | 0.26 (–0.38 to 0.91) |
| Respiratory | Low | 8.9 | 0.36 (0.00 to 0.72) | 1.54 (0.43 to 2.66) | 1.59 (0.57 to 2.62) | 0.20 (–0.74 to 1.16) |
| | High | 5.4 | 0.02 (–0.43 to 0.47) | 0.73 (–0.61 to 2.09) | 0.34 (–0.89 to 1.60) | 0.27 (–0.86 to 1.41) |

[a]We used current day temperature and humidity (lag 0) and 2-day moving average of air pollutants concentrations (lag 01) and we applied 3 df to temperature and humidity. *Significantly different from high educational attainment ($p < 0.05$).

Jerrett et al. 2004). In contrast, Gouveia and Fletcher (2000) observed a larger effect of air pollution in areas of higher SES level; Bateson and Schwartz (2004) found no indication that susceptibility to air pollution varied by group-level SES measures. In the present study, using individual-level education as a measure of SES, we found that residents with low educational attainment were more sensitive to air pollution exposure than those with high educational attainment. Our results provide the first evidence in Mainland China that lower SES may compose a risk factor for air pollution–related health effects.

SES factors such as educational attainment may modify the health effects of outdoor air pollution in several pathways. People with lower SES may be more sensitive to air pollution–related health hazards because they have a higher prevalence of preexisting diseases that confer a greater risk of dying associated with air pollution exposure, and they may also receive inferior medical treatment for preexisting diseases. Disadvantaged living conditions may contribute to the modification effect; people with lower SES may have more limited access to fish, fresh fruits, and vegetables, resulting in reduced intake of antioxidant polyunsaturated fatty acids and vitamins that may protect against adverse consequences of particle exposure (Romieu et al. 2005). Additionally, exposure patterns may contribute to effect modification by SES. Persons with lower SES are less likely to have air conditioning (Long et al. 2007) and more likely to live near busy roadways and have coexposures due to either poor housing or occupation. For example, disadvantaged groups have been found to be more highly exposed to some air pollutants (Sexton et al. 1993). Scandinavian studies have shown differential personal exposures to particles and other pollutants by education and occupation (Rotko et al. 2000, 2001), and a study in the U.S. Great Lakes region indicates differences in exposure to gaseous pollutants by occupation and education, minority status, and income (Pellizzari et al. 1999). Finally, as Jerrett et al. (2004) pointed out, persons with lower education are less mobile and experience less exposure measurement error, thereby reducing bias toward the null.

The limitations of our analysis should be noted. As in other studies in this field, we used available outdoor monitoring data to represent the population exposure to air pollutants. Our assessment of weather conditions was derived entirely from one monitoring station. Measurement error may have substantial implications for interpreting epidemiologic studies on air pollution, particularly for the time-series design (Zeger et al. 2000). It is possible that this type of error may introduce bias to the results of our analysis; however, because of lack of available information on personal exposure to air pollutants, we could not quantify such a bias. Compared with other studies in Europe and North America, the data we collected were limited in being only one city, in sample size, and in duration. In addition, high correlation between particulate matter and gaseous pollutants in Shanghai limited our ability to separate the independent effect for each pollutant.

In summary, in this time-series analysis, we found that outdoor air pollution was associated with mortality from all causes and from cardiopulmonary diseases in Shanghai during 2001–2004. Furthermore, our results suggest that season and sociodemographic factors (e.g., sex, age, SES) may modify the acute health effects of air pollution. These findings provide new information about the effects of modifiers on the relationship between daily mortality and air pollution in developing countries and may have implications for local environmental and social policies.

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# The Effects of Air Pollution on Mortality in Socially Deprived Urban Areas in Hong Kong, China

*Chit-Ming Wong,[1] Chun-Quan Ou,[1,2] King-Pan Chan,[1] Yuen-Kwan Chau,[1] Thuan-Quoc Thach,[1] Lin Yang,[1] Roger Yat-Nork Chung,[1] Graham Neil Thomas,[1] Joseph Sriyal Malik Peiris,[3] Tze-Wai Wong,[4] Anthony Johnson Hedley,[1] and Tai-Hing Lam[1]*

[1]Department of Community Medicine, School of Public Health, The University of Hong Kong, Hong Kong, China; [2]School of Public Health and Tropical Medicine, Southern Medical University, China; [3]Department of Microbiology, The University of Hong Kong, Hong Kong, China; [4]Department of Community and Family Medicine, Chinese University of Hong Kong, Hong Kong, China

**Background:** Poverty is a major determinant of population health, but little is known about its role in modifying air pollution effects.

**Objectives:** We set out to examine whether people residing in socially deprived communities are at higher mortality risk from ambient air pollution.

**Methods:** This study included 209 tertiary planning units (TPUs), the smallest units for town planning in the Special Administrative Region of Hong Kong, China. The socioeconomic status of each TPU was measured by a social deprivation index (SDI) derived from the proportions of the population with *a*) unemployment, *b*) monthly household income < US$250, *c*) no schooling at all, *d*) one-person household, *e*) never-married status, and *f*) subtenancy, from the 2001 Population Census. TPUs were classified into three levels of SDI: low, middle, and high. We performed time-series analysis with Poisson regression to examine the association between changes in daily concentrations of ambient air pollution and daily number of deaths in each SDI group for the period from January 1996 to December 2002. We evaluated the differences in pollution effects between different SDI groups using a case-only approach with logistic regression.

**Results:** We found significant associations of nitrogen dioxide, sulfur dioxide, particulate matter with aerodynamic diameter < 10 μm, and ozone with all nonaccidental and cardiovascular mortality in areas of middle or high SDI ($p < 0.05$). Health outcomes, measured as all nonaccidental, cardiovascular, and respiratory mortality, in people residing in high SDI areas were more strongly associated with $SO_2$ and $NO_2$ compared with those in middle or low SDI areas.

**Conclusions:** Neighborhood socioeconomic deprivation increases mortality risks associated with air pollution.

**Key words:** air pollution, case-only approach, deprivation, effect modification, Hong Kong, mortality, time-series analysis. *Environ Health Perspect* 116:1189–1194 (2008). doi:10.1289/ehp.10850 available via *http://dx.doi.org/* [Online 9 July 2008]

There is ample evidence that air pollution is a health hazard both in developed (Samet et al. 2000) and developing countries [Health Effects Institute (HEI) 2004]. Although all individuals are exposed to some level of air pollution, those who are already in poor health (Bateson and Schwartz 2004; Sunyer et al. 2000) and those who are socially disadvantaged (Forastiere et al. 2006; Jerrett et al. 2004; Neidell 2004) are most strongly affected. Globalization has resulted in the shifting of industries notorious for their pollution from wealthier to poorer areas, where costs of production are cheaper and environmental regulations are less stringent (Pulido 2000). Disparities in environmental health hazards among countries have become greater. In areas near sources of pollution, particularly those with mixed residential and industrial activity and an economically disadvantaged population, residents are exposed to higher levels of air pollution (Finkelstein et al. 2005). This situation has aroused concerns about social injustice, and governments have been urged to take social inequality into account when considering air quality interventions. Studies in Europe and the United States have indicated a link between air pollution and poverty in terms of health impacts (Filleul et al. 2004; Schwartz 2000; Zanobetti and Schwartz 2000). In the Asia Pacific region, where air pollution and the burden of potentially avoidable morbidity and mortality are increasing (HEI 2004), no study has examined the interaction between socioeconomic status and pollution-related health outcomes.

The biologic mechanisms underlying the health effects of air pollution can be explained in terms of oxidative stress and immune system damage after both long- and short-term exposures. There are two main hypotheses regarding the possible effect of the interactions between air pollution and socioeconomic status on health. First, people of lower socioeconomic status are more likely to live and work in places with more toxic pollution. An alternative hypothesis is that because of inadequate access to medical care, lack of material resources, poorer nutrition, and higher smoking prevalence, those of lower socioeconomic status may be more susceptible to the adverse effects of air pollution than those in higher socioeconomic groups (O'Neill et al. 2003).

Health effects associated with socioeconomic factors can be assessed at both the individual and neighborhood levels according to an individual's area of residence. The effect modification of air pollution by socioeconomic status measured at the individual level has been demonstrated in several epidemiologic studies (Filleul et al. 2004; HEI 2000; Krewski et al. 2005). However, the possible modification of air pollution effects associated with socioeconomic status, assessed at the neighborhood level, has not been well studied, and findings are still controversial (O'Neill et al. 2003). Whether residence in socially deprived areas is a greater environmental health hazard compared with residence in better-off areas is an important public health issue, and the possible effects need to be examined through appropriately designed studies.

Hong Kong is an affluent area in the Asia Pacific region, but poverty is still a problem among some subgroups of the population, resulting in serious social inequity. Socially deprived areas should be identified for additional community environmental protection and health resource allocation. Socioeconomic factors are usually multidimensional, and some of them, such as low income and low education, may be correlated with each other. Instead of studying several factors individually, we used a deprivation score at a specific community planning unit level to estimate neighborhood

Address correspondence to A.J. Hedley, School of Public Health, The University of Hong Kong, 5th Floor, William MW Mong Block, Faculty of Medicine Building, 21 Sassoon Road, Hong Kong SAR, China. Telephone: (852) 2819-9282. Fax: (852) 2855-9528. E-mail: hrmrajh@hkucc.hku.hk

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social deprivation for each of the subjects based on geographic code of their residency at the time of death, then assessed whether residents in poorer areas were subject to greater risk of mortality from ambient air pollution.

## Materials and Methods

***Tertiary planning units (TPUs).*** The TPU system was devised by the Hong Kong Planning Department for town planning purposes. In 2001, the whole land area of Hong Kong was divided into 276 TPUs. Our analysis included all TPUs except for suburban TPUs ($n$ = 67) in the New Territories and outer islands of Hong Kong, which are remote and have population densities lower than the lowest quartile (533/km$^2$) of the whole territory. People residing in these sparsely populated areas account for about 1.5% of the total population and are usually exposed to sources and levels of air pollution different from those in urban areas. Because air pollution exposure measurements were based on data from monitoring stations located in urban areas, exclusion of nonurban areas would reduce exposure measurement errors.

***Measures of social deprivation.*** The Census and Statistics Department of Hong Kong conducts a population census every 10 years and a by-census every intermediate 5 years. TPUs are the smallest units in the population census report. The 2001 census report contains 44 statistics of the Hong Kong population measured at TPU level. We performed factor analysis on 18 socioeconomic and demographic variables related to social deprivation available in this population census database. Six factors accounting for 69% of the variation were extracted from principal-component analysis. Based on the distribution of factor loadings, we chose six variables to describe the conditions of social deprivation for each TPU: the proportions of the population with *a*) unemployment, *b*) monthly household income < US$250, *c*) no schooling at all, *d*) one-person household, *e*) never-married status, and *f*) subtenancy. Each of these six variables had significant factor loading for a specific principal factor, and all of them are deemed to be representative indicators of social disadvantage in the published literature and in the setting of the Hong Kong population. The first four conditions are more or less related to a lack of material resources. Being unmarried in Chinese society would have been regarded previously as undesirable in a social and family context. In Hong Kong, people who cannot afford to rent a whole flat may rent a part (usually a small room) of a flat from another tenant. The six selected variables in this study are similar to those used in other well-known social deprivation indices in other countries such as Index of Local Conditions (Department of Environment 1994) and the Jarman (Jarman 1983), and Townsend (Benach et al. 2001; Payne et al. 1996; Townsend et al. 1988) indices. For example, the "unemployment proportion" is similar to "unemployment rate"; "subtenancy" is similar to "not owner-occupier households"; "never married" is a dimension similar to "lone parent household"; "one-person household" could indicate partly "lone pensioner"; and "no school" is broadly similar to "low secondary education attainment" (Benach et al. 2001; Payne et al. 1996).

The social deprivation index (SDI) for each TPU was calculated by taking the average of these six selected variables. A detailed description of the development of SDI is given in one of our previous studies (Wong et al. 1999), which showed that each of these six measures was correlated with standard mortality rate at TPU level and mortality was high in TPUs with high SDI. Based on tertiles of SDI, all TPUs were classified into one of three SDI groups: low (less than the lowest tertile of SDI), middle (the lowest tertile to the middle tertile), and high (greater than the highest tertile). Table 1 shows a summary of basic characteristics for the 209 urban TPUs by SDI level.

***Health outcomes.*** The Census and Statistics Department of Hong Kong provided mortality data for all registered deaths from January 1996 to December 2002, including age, sex, date of death, TPU of residence, and the code of underlying cause of death, which is classified according to the *International Classification of Diseases, 9th Revision* (ICD-9), 1996–1999 and *10th Revision* (ICD-10), 2000–2002 (World Health Organization 1977, 1992). For each SDI group, we aggregated daily numbers of deaths due to all nonaccidental causes (ICD-9 codes 001-799; ICD-10 codes A00-T99, Z00-Z99), cardiovascular (ICD-9 390-459; ICD-10 I00-I99) and respiratory (ICD-9 460-519; ICD-10 J00-J98) diseases, respectively.

***Air pollution and meteorologic data.*** Hourly concentrations of nitrogen dioxide, sulfur dioxide, particulate matter with aerodynamic diameter < 10 μm ($PM_{10}$), and ozone were derived from eight fixed-site general monitoring stations operated by the Environmental Protection Department (HK EPD 2007). The measurement methods for $NO_2$, $SO_2$, $PM_{10}$, and $O_3$ were chemiluminescence, fluorescence, tapered element oscillating microbalance, and ultraviolet absorption, respectively. $NO_2$, $SO_2$, and $O_3$ were also measured by differential optical absorption spectroscopy in some monitoring stations. Daily concentrations of air pollutants for each monitoring station were taken to be the average of the 24-hr concentrations of $NO_2$, $SO_2$, and $PM_{10}$ and of 8-hr (0100–1800 hours) concentrations of $O_3$. Daily concentrations of air pollutants for the whole territory of Hong Kong were evaluated by averaging the daily concentrations across all monitoring stations using the method of centering (Wong et al. 2001). In calculating the daily data there should be at least 75% 1-hr values of that particular day, and for each monitoring station there should be at least 75% of daily data complete for the whole study period. Meteorologic data, including daily temperature and relative humidity, were provided by the Hong Kong Observatory (2007).

***Statistical methods.*** We used generalized linear modeling to obtain the most adequate core models for each health outcome. We used

**Table 1.** Summary statistics for TPUs by three levels of social deprivation, air pollution, and meteorologic variables for whole territories.

| Variable | Min | 1st Quartile | Median | 3rd Quartile | Max | Mean | SD |
|---|---|---|---|---|---|---|---|
| Population size (× 10,000) | | | | | | | |
| Low SDI | 0.40 | 1.19 | 2.32 | 5.75 | 18.99 | 4.22 | 4.19 |
| Middle SDI | 0.12 | 1.05 | 4.86 | 7.11 | 20.36 | 5.25 | 4.86 |
| High SDI | 0.11 | 0.76 | 1.42 | 2.52 | 8.63 | 2.07 | 1.99 |
| Area (km$^2$) | | | | | | | |
| Low SDI | 0.13 | 0.83 | 1.82 | 4.54 | 14.08 | 3.33 | 3.45 |
| Middle SDI | 0.13 | 0.81 | 1.62 | 3.05 | 35.61 | 3.43 | 6.37 |
| High SDI | 0.06 | 0.38 | 0.79 | 2.43 | 16.30 | 2.56 | 4.00 |
| Population density (× 10,000/km$^2$) | | | | | | | |
| Low SDI | 0.09 | 0.55 | 1.68 | 3.80 | 16.75 | 2.49 | 2.76 |
| Middle SDI | 0.04 | 0.46 | 3.06 | 6.40 | 15.48 | 4.23 | 4.03 |
| High SDI | 0.05 | 0.28 | 2.52 | 6.02 | 17.95 | 3.75 | 4.14 |
| Mortality (daily count) | | | | | | | |
| Low SDI | 5.0 | 16.0 | 19.0 | 23.0 | 46.0 | 19.3 | 5.3 |
| Middle SDI | 13.0 | 31.0 | 36.0 | 42.0 | 66.0 | 36.2 | 8.0 |
| High SDI | 3.0 | 13.0 | 17.0 | 21.0 | 40.0 | 17.4 | 5.4 |
| Air pollutants (μg/m$^3$) | | | | | | | |
| $NO_2$ | 10.1 | 45.1 | 56.3 | 69.6 | 168.0 | 58.7 | 20.0 |
| $SO_2$ | 1.8 | 9.6 | 14.7 | 22.1 | 109.4 | 17.8 | 12.1 |
| $PM_{10}$ | 13.5 | 31.8 | 45.5 | 66.7 | 188.5 | 51.6 | 25.3 |
| $O_3$ | –8.2 | 19.2 | 31.7 | 50.8 | 196.6 | 36.9 | 23.0 |
| Temperature (°C) | 6.9 | 19.8 | 24.7 | 27.8 | 33.8 | 23.7 | 4.9 |
| Relative humidity (%) | 27.0 | 74.0 | 79.0 | 84.0 | 97.0 | 77.9 | 10.0 |

Abbreviations: Max, maximum; Min, minimum.

Poisson regression with quasi-likelihood method to model mortality and hospital admission counts with adjustment for overdispersion (McCullagh and Nelder 1989). To control for systematic variation over time, we introduced a trend and seasonality term and dummy variables for day of the week and public holidays. Other covariates considered and adjusted for were daily mean temperature and relative humidity. The trend and seasonality term was defined by fitting a natural smoothing spline with 4–6 degrees of freedom (dfs) per year. Additional smoothing splines with 3 dfs were included to adjust for the effects of temperature and 3 dfs to adjust for relative humidity. The choice of the number of dfs for each smoothing function was made on the basis of observed autocorrelations for the residuals using partial autocorrelation function plots. Partial autocorrelation coefficient (Hastie and Tibshirani 1990) of $|\rho| < 0.1$ for the first 2 lag days was used as a criterion for a minimally adequate model. Randomness of residuals and autoregressive terms were also considered in selecting the most appropriate models. If the above criteria were met, the variable for the air pollutant concentrations was entered into the core model for assessment of percentage excess risk (ER) per 10-μg/m$^3$ increase of an air pollutant at single lag 0–4 days and at average lag 0 and lag 1 day. We performed Poisson regression analysis and assessed the ER for each level of social deprivation in the data set stratified by level of social deprivation. All analyses under Poisson regression were performed using the statistical software package R version 2.5.1 (R Development Core team 2006) with mgcv package version 1.3-25.

In addition, we used a case-only approach in a combined data set to assess potential interaction between social deprivation level and ambient air pollution on mortality. The case-only approach with logistic regression was originally proposed for studying the gene–environment interaction and has been widely used in this field of study (Fallin et al. 2003; Fracanzani et al. 2005). Armstrong (2003) has pointed out that this method can be extended for evaluating the interaction between time-varying variables and individual factors. Subsequently, Schwartz (2005) gave a more detailed description of this method and applied it to examine whether medical conditions modify the mortality effects of extreme temperature. We used this method recently to examine the effect modification of air pollution by individual smoking status and physical activity (Wong et al. 2007a, 2007b). In the present study, we assume that the risk of dying associated with temporary increase in air pollution level is modified by residence in different social deprivation areas. For example, people who died on days with high levels of air pollution would be more likely to reside in a high SDI area than those who died on days with low levels of air pollution, and therefore the air pollution level at the date of death could be a predictor of neighborhood SDI level of the deceased using logistic regression. The difference in relative risk of mortality associated with air pollution between SDI levels was calculated based on the relationship between SDI and the levels of ambient air pollution using multinomial logistic regression. Furthermore, an ordinal logit model was fitted to determine whether there was a trend in the health effects of air pollution increasing from low to middle and then to high SDI levels.

## Results

Figure 1 shows the geographic variations in social deprivation in the whole of Hong Kong excluding suburban areas. Most of the areas with high SDI levels were in the northern territories bordering mainland China and in the outer islands. There were also a few highly deprived areas in the inner city.

***Health outcomes and covariates.*** Our study included a total of 215,240 nonaccidental deaths (males: 120,262; females: 94,978) from 1996 to 2002, with an average of 30,749 deaths per year. Summary statistics were compiled for daily counts of deaths from nonaccidental causes and from cardiovascular and respiratory diseases as well as daily meteorologic conditions and concentrations of the four air pollutants under study (Table 1). On each day there were, on average, 19, 36, and 17 deaths from nonaccidental causes in the TPUs among low, middle, and high SDI levels, respectively.

***Effects of air pollution for all areas.*** In all areas, for nonaccidental and subcategory cardiovascular causes of mortality, the biggest single-day associations with all air pollutants occurred at either lag 0 or lag 1 day (Tables 2

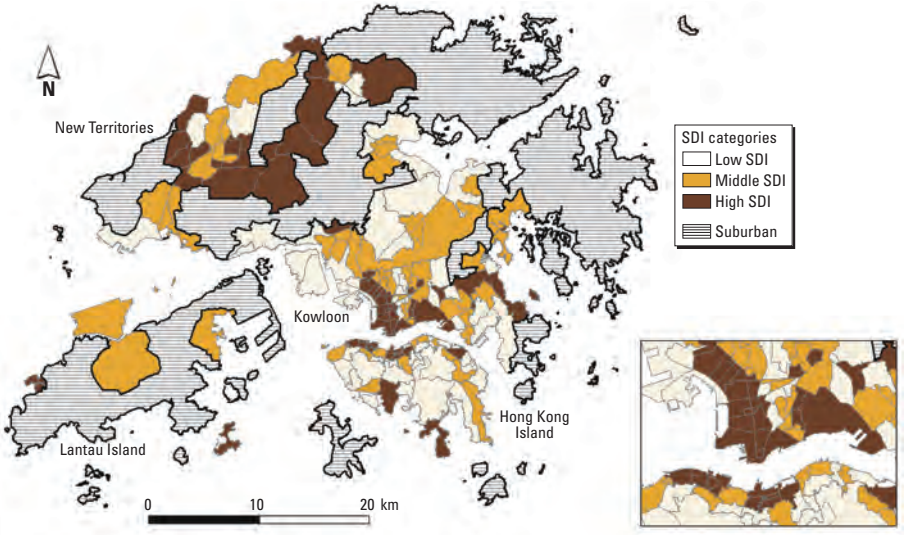


**Figure 1.** SDI in three levels for Hong Kong, 2001, excluding suburban areas.

**Table 2.** Excess risk (%) of nonaccidental mortality per 10-μg/m$^3$ increase in pollutant concentration by three levels of social deprivation at lag 0, 1, 2, 3, and 4 days.

| | Lag | Low SDI ER (95% CI) | Middle SDI ER (95% CI) | High SDI ER (95% CI) | All areas ER (95% CI) |
|---|---|---|---|---|---|
| $NO_2$ | 0 | 0.55 (0.00 to 1.11) | 1.07 (0.65 to 1.50) | 0.53 (–0.06 to 1.13) | 0.75 (0.45 to 1.06) |
| | 1 | 0.40 (–0.15 to 0.95) | 1.04 (0.61 to 1.46) | 1.07 (0.48 to 1.66) | 0.79 (0.49 to 1.10) |
| | 2 | 0.16 (–0.37 to 0.70) | 0.62 (0.21 to 1.04) | 0.52 (–0.05 to 1.10) | 0.37 (0.07 to 0.67) |
| | 3 | 0.29 (–0.24 to 0.82) | 0.39 (–0.03 to 0.80) | 0.12 (–0.45 to 0.70) | 0.20 (–0.10 to 0.50) |
| | 4 | –0.30 (–0.82 to 0.24) | 0.12 (–0.29 to 0.53) | –0.22 (–0.79 to 0.36) | –0.12 (–0.41 to 0.18) |
| $SO_2$ | 0 | 0.64 (–0.16 to 1.44) | 0.76 (0.14 to 1.38) | 0.81 (–0.05 to 1.68) | 0.68 (0.24 to 1.12) |
| | 1 | 0.21 (–0.57 to 1.00) | 0.62 (0.02 to 1.23) | 1.44 (0.60 to 2.29) | 0.62 (0.19 to 1.06) |
| | 2 | 0.23 (–0.53 to 1.01) | 0.34 (–0.26 to 0.93) | 0.33 (–0.50 to 1.17) | 0.20 (–0.23 to 0.63) |
| | 3 | 0.15 (–0.61 to 0.92) | 0.14 (–0.45 to 0.74) | –0.45 (–1.28 to 0.38) | –0.10 (–0.53 to 0.32) |
| | 4 | –0.70 (–1.46 to 0.07) | 0.18 (–0.41 to 0.77) | –0.55 (–1.38 to 0.28) | –0.24 (–0.66 to 0.18) |
| $PM_{10}$ | 0 | 0.37 (–0.10 to 0.84) | 0.70 (0.34 to 1.07) | 0.22 (–0.29 to 0.73) | 0.45 (0.19 to 0.72) |
| | 1 | 0.40 (–0.04 to 0.84) | 0.48 (0.14 to 0.82) | 0.46 (–0.01 to 0.94) | 0.40 (0.15 to 0.64) |
| | 2 | 0.14 (–0.28 to 0.57) | 0.35 (0.02 to 0.68) | 0.29 (–0.17 to 0.75) | 0.22 (–0.02 to 0.45) |
| | 3 | –0.12 (–0.55 to 0.30) | 0.18 (–0.14 to 0.51) | –0.05 (–0.51 to 0.40) | 0.00 (–0.24 to 0.23) |
| | 4 | –0.14 (–0.56 to 0.28) | 0.17 (–0.16 to 0.50) | –0.06 (–0.51 to 0.40) | 0.03 (–0.20 to 0.26) |
| $O_3$ | 0 | –0.20 (–0.73 to 0.34) | 0.41 (0.00 to 0.82) | 0.53 (–0.04 to 1.11) | 0.23 (–0.07 to 0.52) |
| | 1 | 0.22 (–0.26 to 0.70) | 0.46 (0.09 to 0.83) | 0.02 (–0.49 to 0.54) | 0.27 (0.00 to 0.53) |
| | 2 | 0.20 (–0.25 to 0.65) | 0.23 (–0.12 to 0.58) | 0.19 (–0.30 to 0.68) | 0.18 (–0.07 to 0.43) |
| | 3 | 0.00 (–0.44 to 0.45) | 0.21 (–0.14 to 0.55) | 0.18 (–0.30 to 0.66) | 0.13 (–0.11 to 0.38) |
| | 4 | –0.17 (–0.60 to 0.27) | 0.04 (–0.29 to 0.38) | –0.03 (–0.50 to 0.45) | –0.02 (–0.27 to 0.22) |

**Table 3.** Excess risk (%) of cardiovascular mortality per 10-μg/m$^3$ increase in pollutant concentration by three levels of social deprivation at lag 0, 1, 2, 3, and 4 days.

| | Lag | Low SDI ER (95% CI) | Middle SDI ER (95% CI) | High SDI ER (95% CI) | All areas ER (95% CI) |
|---|---|---|---|---|---|
| $NO_2$ | 0 | 0.82 (–0.25 to 1.90) | 1.24 (0.45 to 2.03) | 1.45 (0.37 to 2.53) | 1.17 (0.61 to 1.73) |
| | 1 | 0.76 (–0.30 to 1.83) | 1.00 (0.22 to 1.78) | 2.14 (1.07 to 3.21) | 1.08 (0.53 to 1.64) |
| | 2 | 0.34 (–0.70 to 1.39) | 0.85 (0.08 to 1.61) | 0.95 (–0.09 to 2.00) | 0.53 (–0.02 to 1.08) |
| | 3 | 0.27 (–0.76 to 1.31) | 0.46 (–0.30 to 1.23) | –0.28 (–1.32 to 0.77) | 0.09 (–0.45 to 0.63) |
| | 4 | –0.51 (–1.54 to 0.52) | 0.08 (–0.67 to 0.84) | 0.02 (–1.01 to 1.06) | –0.13 (–0.66 to 0.41) |
| $SO_2$ | 0 | 1.10 (–0.45 to 2.68) | 0.71 (–0.44 to 1.87) | 1.85 (0.28 to 3.44) | 1.03 (0.21 to 1.85) |
| | 1 | 0.89 (–0.64 to 2.44) | 0.30 (–0.83 to 1.45) | 2.88 (1.35 to 4.43) | 0.93 (0.13 to 1.74) |
| | 2 | 0.38 (–1.12 to 1.90) | 0.36 (–0.75 to 1.48) | 1.28 (–0.22 to 2.81) | 0.42 (–0.37 to 1.21) |
| | 3 | 0.26 (–1.23 to 1.77) | 0.25 (–0.85 to 1.37) | 0.06 (–1.45 to 1.58) | 0.10 (–0.69 to 0.89) |
| | 4 | –0.75 (–2.24 to 0.76) | –0.27 (–1.36 to 0.85) | 0.66 (–0.84 to 2.19) | –0.21 (–1.00 to 0.58) |
| $PM_{10}$ | 0 | 0.14 (–0.77 to 1.06) | 0.66 (0.00 to 1.34) | 0.83 (–0.08 to 1.75) | 0.52 (0.05 to 1.00) |
| | 1 | 0.64 (–0.21 to 1.49) | 0.49 (–0.13 to 1.12) | 0.89 (0.04 to 1.75) | 0.58 (0.14 to 1.03) |
| | 2 | 0.24 (–0.58 to 1.07) | 0.80 (0.20 to 1.40) | 0.12 (–0.70 to 0.95) | 0.43 (0.00 to 0.86) |
| | 3 | –0.27 (–1.09 to 0.55) | 0.65 (0.06 to 1.25) | –0.09 (–0.91 to 0.73) | 0.14 (–0.28 to 0.57) |
| | 4 | 0.01 (–0.80 to 0.83) | 0.52 (–0.07 to 1.12) | 0.04 (–0.77 to 0.86) | 0.23 (–0.20 to 0.65) |
| $O_3$ | 0 | 0.23 (–0.81 to 1.29) | 0.57 (–0.19 to 1.35) | 0.66 (–0.39 to 1.72) | 0.42 (–0.12 to 0.97) |
| | 1 | 0.41 (–0.53 to 1.35) | 0.65 (–0.04 to 1.34) | 0.23 (–0.71 to 1.18) | 0.45 (–0.04 to 0.94) |
| | 2 | 0.51 (–0.37 to 1.40) | 0.52 (–0.13 to 1.17) | 0.23 (–0.66 to 1.13) | 0.38 (–0.08 to 0.84) |
| | 3 | 0.51 (–0.35 to 1.39) | 0.55 (–0.09 to 1.19) | –0.17 (–1.04 to 0.71) | 0.28 (–0.17 to 0.74) |
| | 4 | –0.29 (–1.15 to 0.58) | 0.02 (–0.61 to 0.66) | –0.51 (–1.37 to 0.37) | –0.23 (–0.68 to 0.22) |

**Table 4.** Excess risk (%) of respiratory mortality per 10-μg/m$^3$ increase in pollutant concentration by three levels of social deprivation at lag 0, 1, 2, 3, and 4 days.

| | Lag | Low SDI ER (95% CI) | Middle SDI ER (95% CI) | High SDI ER (95% CI) | All areas ER (95% CI) |
|---|---|---|---|---|---|
| $NO_2$ | 0 | 1.02 (–0.31 to 2.36) | 0.76 (–0.20 to 1.72) | 0.97 (–0.34 to 2.30) | 0.88 (0.19 to 1.58) |
| | 1 | 0.16 (–1.16 to 1.49) | 1.07 (0.13 to 2.03) | 1.26 (–0.04 to 2.57) | 0.90 (0.22 to 1.60) |
| | 2 | –0.05 (–1.34 to 1.26) | 1.02 (0.10 to 1.96) | 1.62 (0.35 to 2.91) | 0.92 (0.25 to 1.60) |
| | 3 | 0.13 (–1.16 to 1.43) | 0.94 (0.02 to 1.87) | 0.95 (–0.32 to 2.23) | 0.75 (0.08 to 1.42) |
| | 4 | –0.53 (–1.81 to 0.77) | 0.51 (–0.40 to 1.44) | –0.30 (–1.56 to 0.98) | 0.05 (–0.62 to 0.72) |
| $SO_2$ | 0 | 1.21 (–0.70 to 3.16) | 0.57 (–0.80 to 1.95) | 1.84 (–0.04 to 3.76) | 1.06 (0.06 to 2.06) |
| | 1 | 0.06 (–1.83 to 1.98) | 1.33 (–0.01 to 2.68) | 1.32 (–0.53 to 3.20) | 1.02 (0.04 to 2.01) |
| | 2 | 0.45 (–1.40 to 2.33) | 1.01 (–0.31 to 2.34) | 1.47 (–0.34 to 3.32) | 0.99 (0.03 to 1.96) |
| | 3 | 0.32 (–1.53 to 2.20) | 1.30 (–0.01 to 2.62) | –0.67 (–2.48 to 1.18) | 0.56 (–0.40 to 1.52) |
| | 4 | –1.36 (–3.21 to 0.53) | 0.77 (–0.54 to 2.10) | –1.05 (–2.87 to 0.81) | –0.21 (–1.17 to 0.76) |
| $PM_{10}$ | 0 | 0.69 (–0.44 to 1.82) | 0.31 (–0.50 to 1.13) | 0.27 (–0.85 to 1.40) | 0.39 (–0.20 to 0.99) |
| | 1 | 0.55 (–0.50 to 1.61) | 0.77 (0.01 to 1.53) | 0.72 (–0.32 to 1.78) | 0.70 (0.15 to 1.26) |
| | 2 | 0.36 (–0.66 to 1.39) | 0.85 (0.12 to 1.59) | 1.46 (0.45 to 2.47) | 0.89 (0.36 to 1.42) |
| | 3 | –0.24 (–1.25 to 0.78) | 0.66 (–0.07 to 1.39) | 0.70 (–0.30 to 1.71) | 0.45 (–0.08 to 0.98) |
| | 4 | –0.17 (–1.17 to 0.85) | 0.69 (–0.03 to 1.42) | 0.48 (–0.52 to 1.48) | 0.43 (–0.10 to 0.96) |
| $O_3$ | 0 | –0.22 (–1.50 to 1.07) | 0.02 (–0.90 to 0.94) | 0.60 (–0.66 to 1.88) | 0.11 (–0.55 to 0.79) |
| | 1 | 0.46 (–0.68 to 1.61) | 0.26 (–0.56 to 1.09) | –0.51 (–1.65 to 0.64) | 0.11 (–0.48 to 0.72) |
| | 2 | –0.01 (–1.09 to 1.09) | 0.50 (–0.28 to 1.28) | 0.42 (–0.65 to 1.51) | 0.36 (–0.21 to 0.93) |
| | 3 | –0.31 (–1.38 to 0.77) | 0.24 (–0.52 to 1.01) | 0.55 (–0.50 to 1.62) | 0.19 (–0.37 to 0.75) |
| | 4 | –0.01 (–1.06 to 1.06) | 0.04 (–0.71 to 0.80) | 0.88 (–0.16 to 1.93) | 0.25 (–0.30 to 0.80) |

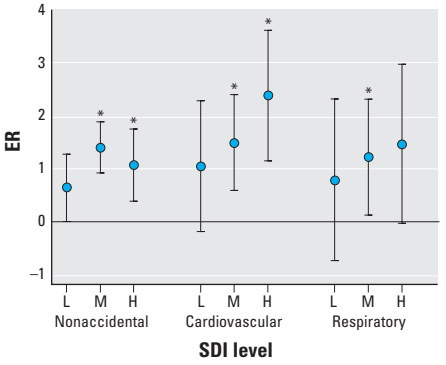


**Figure 2.** ER of mortality from nonaccidental, cardiovascular, and respiratory per 10-μg/m$^3$ increase in $NO_2$ concentration by three levels [low (L), middle (M), and high (H)] of social deprivation at average 0–1 lag day. Error bars indicate 95% CIs of estimates of ER.
*$p < 0.05$.

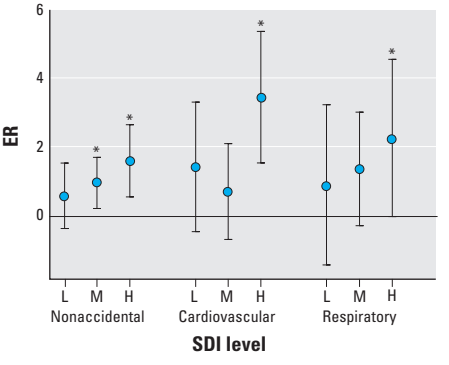


**Figure 3.** ER of mortality from nonaccidental, cardiovascular, and respiratory per 10 μg/m$^3$ increase in $SO_2$ concentration by three levels [low (L), middle (M), and high (H)] of social deprivation at average 0–1 lag day. Error bars indicate 95% CIs of estimates of ER.
*$p < 0.05$.

and 3), but for subcategory respiratory mortality, they occurred at lag 2 day except with $SO_2$, which occurred at lag 0 day (Table 4). There were statistically significant ($p < 0.05$) ERs for all the pollutants except $O_3$ on all the three mortality outcomes.

***Separate effects of air pollution for each SDI group.*** The lag patterns of ER were comparable in the high, middle, and low SDI groups (Table 2). At average 0–1 lag—that is, with average pollutant concentration measured in the lag 0–1 day period—for $NO_2$ and $SO_2$, the point estimates of ER were higher in the middle SDI than in the low SDI group, except for $SO_2$ for cardiovascular mortality, and were the highest in the high SDI group, except for $NO_2$ for nonaccidental mortality (Figure 2). At average 0–1 lag, for $PM_{10}$ and $O_3$ the point estimates of ER were higher in the middle SDI than in the low SDI group (data not shown). Those in the high SDI group were higher than in the low SDI group (except the effect of $PM_{10}$ on nonaccidental mortality). For respiratory mortality, at average 0–1 lag, for $NO_2$ and $SO_2$ the point estimates of ER increased from low to high SDI groups (Figures 2 and 3), with ER increasing from 0.76 to 1.44% for $NO_2$ (Figure 2), and from 0.90 to 2.27% for $SO_2$ (Figure 3). However, for $PM_{10}$ and $O_3$, the point estimates of ER varied from low to high SDI groups by only a small magnitude (0.82 to 0.70% for $PM_{10}$; 0.23 to 0.0% for $O_3$) (data not shown).

***Differences in effects of air pollution between SDI groups.*** The biggest difference in ER between SDI groups generally occurred at lag 1 day (data not shown). For nonaccidental mortality and for the subcategory cardiovascular mortality, the ER due to $NO_2$ and $SO_2$ at lag 1 day was significantly higher ($p < 0.05$) in the high SDI group than in the middle or low SDI groups; and the trends from low to high SDI groups were significant ($p < 0.05$) (data not shown). At the average 0–1 lag of a pollutant per 10 μg/m$^3$, significantly ($p < 0.05$) greater ER for nonaccidental mortality, between high and middle SDI groups [change in ER 1.15%; 95% confidence interval (CI) 0.06–2.26] and between high and low (change in ER 1.38%; 95% CI, 0.13–2.63) SDI groups were shown (Table 5). Significant trend (change in ER 0.45%; 95% CI, 0.03–0.87) with change between middle and low or between high and middle SDI groups were found for an increase in concentrations of $SO_2$, but not in concentrations of the other pollutants, although the differences in ER were in the same direction as that for $SO_2$. For effects on cardiovascular mortality, significant increases ($p < 0.05$) in ER were found for $SO_2$ (between high and middle SDI groups) and for $NO_2$ (between high and low SDI groups); and significant trend ($p < 0.05$) was found for

$NO_2$. The magnitude of the difference and trend between SDI groups in effects of all pollutants on respiratory mortality were similar to those on all nonaccidental mortality but were statistically not significant ($p > 0.05$).

## Discussion

In Hong Kong, we found that air pollution mortality effects for $SO_2$ were stronger in high compared with low SDI areas. Some previous studies in Hong Kong (Wong et al. 2001, 2002a) and Mainland China (Kan and Chen 2003; Venners et al. 2003; Xu et al. 1994, 1995) showed the gaseous pollutants $NO_2$ and $SO_2$ had stronger effects on morbidity and mortality compared with particulate air pollution in contrast to the findings in the United States (Samet et al. 2000). In this study, in addition to $SO_2$ we found those residing in high SDI areas had higher ERs of death also associated with $NO_2$, particularly for cardiovascular disease, than those in low SDI areas. A possible explanation is that socially deprived subgroups are more likely to have poorer health care and nutrition and other increased health risks, resulting in increased susceptibility to the adverse effects of air pollution. A meta-analysis of short-term health effects of air pollution ($SO_2$, $NO_2$, CO, $PM_{10}$, and $O_3$) in eight Italian cities showed that the ERs for hospital admission were modified by deprivation score and by $NO_2/PM_{10}$ ratio (Biggeri et al. 2005). Another explanation is that those residing in higher SDI areas may be exposed to higher levels of $NO_2$ and $SO_2$. A study in the Hamilton Census Metropolitan Area, Canada (Finkelstein et al. 2005), showed that subjects in the more deprived neighborhoods were exposed to higher levels of ambient particulates and gaseous pollutants. At least some of the observed social gradients associated with circulatory mortality arise from inequalities in environmental factors in terms of exposure to background and traffic-related pollutants. In Hong Kong, the daily levels of $PM_{10}$ with correlations ($r$) between the eight monitoring stations ranged from 0.9 to 1.0 and annual average concentration from 42 to 55 μg/m$^3$, indicating the homogeneity of $PM_{10}$ exposure between SDI areas. However, the corresponding levels for $NO_2$ ranged from 45 to 67 μg/m$^3$ ($r$ = 0.5–0.9), and 8–16 μg/m$^3$ for $SO_2$ ($r$ = 0.4–0.8). The difference in the levels of $NO_2$ and $SO_2$ across geographic areas may partly explain the significant differences in their effects between SDI areas. On the other hand, in Hong Kong a large proportion of ambient air pollution is attributable to pollution emissions from road traffic (Wong et al. 2002b). Many deprived areas are located in the inner city on multiple busy traffic routes. Most of the population live next to roads and are affected by street canyon effects commonly formed by continuous building blocks in Hong Kong (Chan and Kwok 2000). In another study, high exposure to carbon monoxide was found to have a significant effect on asthma admissions for children 1–18 years of age, and the effect was greater for children with lower socioeconomic status (Neidell 2004).

In six regions of São Paulo City, Brazil, $PM_{10}$ effects on daily respiratory deaths at the region level were negatively correlated with both the percentage of people with college education and high family income and were positively associated with the percentage of people living in slums, suggesting that social deprivation represents an effect modifier of the association between air pollution and respiratory deaths (Martins et al. 2004). In the city of Hamilton, Ontario, Canada, which was divided into five zones based on proximity to fixed-site air pollution monitors, $SO_2$ and coefficient of haze (as a measure of particulate pollution) were associated with increased mortality, and the effects were higher among those zones with lower socioeconomic characteristics, lower educational attainment, and higher manufacturing employment (Jerrett et al. 2004).

There are several limitations to our study. First, we are aware that the SDI we defined may not reflect the whole profile of deprivation, although all of the information available from the census is included in the computation. Second, there may be heterogeneity within areas having the same SDI levels that have not been accounted for. However, we classified SDI levels into three broad categories, which should help reduce misclassification of deprivation. Third, population-level exposures using average concentrations from a limited number of air pollution monitors as a proxy for each individual may be subject to some measurement errors, and consequently we cannot determine whether the increased pollution-related mortality risk in high SDI areas is due mainly to greater pollutant exposure or increased biologic susceptibility. However, the population density in Hong Kong is very high (about 6,200/km$^2$), and the daily air pollution levels among eight monitoring stations included in the study were highly correlated. This justifies our use of the average air pollution concentrations over all monitoring stations as daily concentrations for the whole territory. The aggregated daily concentrations derived for the whole of Hong Kong should be at least as reliable as measurements used in other daily time-series air pollution studies. In this study, we used $PM_{10}$ to assess the effect of particulate pollution, because the measurements of $PM_{2.5}$ were not available in all the stations under study during the period of the study. However, based on the available data from two stations, the Spearman correlation coefficient between daily levels of the two measures was 0.89, and $PM_{2.5}$ constituted a high proportion of $PM_{10}$ (around 70%); therefore, it is unlikely that estimates using the two measures would differ to a great extent in Hong Kong. Unlike specific gaseous pollutants that are comparable from place to place, the potency of $PM_{10}$ will depend on the composition of the particulates, which may vary greatly in different geographic locations. The comparability of air pollution studies on health effects of particulates may be related more to specific subspecies than the particle size measured. Finally, the mechanisms underlying why some population groups with high SDI experienced higher adverse effects of air pollution are still unclear, and research on specific protective interventions is needed.

**Table 5.** Difference in ER [% (95% CI)] of mortality between areas with different SDI levels associated with air pollutants per 10-μg/m$^3$ increase at average lag 0–1 day.

| | Pollutant | Nonaccidental causes | Cardiovascular disease | Respiratory disease |
|---|---|---|---|---|
| High vs. middle | $NO_2$ | 0.45 (–0.16 to 1.06) | 1.03 (–0.11 to 2.18) | 0.94 (–0.41 to 2.31) |
| | $SO_2$ | 1.15 (0.06 to 2.26) | 2.74 (0.66 to 4.85) | 1.62 (–0.83 to 4.12) |
| | $PM_{10}$ | 0.23 (–0.25 to 0.72) | 0.49 (–0.40 to 1.40) | 0.49 (–0.58 to 1.58) |
| | $O_3$ | 0.14 (–0.41 to 0.70) | 0.09 (–0.95 to 1.14) | 0.75 (–0.50 to 2.01) |
| High vs. low | $NO_2$ | 0.51 (–0.18 to 1.20) | 1.35 (0.49 to 2.67) | 0.59 (–0.98 to 2.18) |
| | $SO_2$ | 1.38 (0.13 to 2.63) | 2.16 (–0.19 to 4.57) | 2.42 (–0.47 to 5.38) |
| | $PM_{10}$ | 0.12 (–0.42 to 0.67) | 0.82 (–0.20 to 1.86) | –0.15 (–1.39 to 1.10) |
| | $O_3$ | 0.14 (–0.48 to 0.76) | 0.13 (–1.06 to 1.33) | 0.33 (–1.12 to 1.79) |
| Trend test | $NO_2$ | 0.16 (–0.07 to 0.39) | 0.45 (0.01 to 0.88) | 0.21 (–0.32 to 0.73) |
| | $SO_2$ | 0.45 (0.03 to 0.87) | 0.71 (–0.08 to 1.51) | 0.81 (–0.15 to 1.71) |
| | $PM_{10}$ | 0.04 (–0.15 to 0.22) | 0.27 (–0.07 to 0.61) | –0.04 (–0.46 to 0.37) |
| | $O_3$ | 0.05 (–0.16 to 0.25) | 0.04 (–0.35 to 0.44) | 0.12 (–0.37 to 0.60) |

## Conclusions

This study provides evidence that neighborhood socioeconomic status plays a role in the association between ambient air pollution and mortality. Residence in areas of high social deprivation may increase the mortality risks associated with air pollution. These findings should promote discussion among scientists, policy makers, and the public about social inequities in health when considering environmental protection and management in the context of economic, urban, and infrastructural development.

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# Public Health and Air Pollution in Asia (PAPA): A Multicity Study of Short-Term Effects of Air Pollution on Mortality

*Chit-Ming Wong,[1] Nuntavarn Vichit-Vadakan,[2] Haidong Kan,[3,4] Zhengmin Qian,[5,6] and the PAPA Project Teams**

[1]Department of Community Medicine, School of Public Health, The University of Hong Kong, Hong Kong Special Administrative Region, China; [2]Faculty of Public Health, Thammasat University, Pathumthani, Thailand; [3]School of Public Health, Fudan University, Shanghai, China; [4]Epidemiology Branch, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA; [5]Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA; [6]Geisinger Center for Health Research, Danville, Pennsylvania, USA

**Background and objectives:** Although the deleterious effects of air pollution from fossil fuel combustion have been demonstrated in many Western nations, fewer studies have been conducted in Asia. The Public Health and Air Pollution in Asia (PAPA) project assessed the effects of short-term exposure to air pollution on daily mortality in Bangkok, Thailand, and in three cities in China: Hong Kong, Shanghai, and Wuhan.

**Methods:** Poisson regression models incorporating natural spline smoothing functions were used to adjust for seasonality and other time-varying covariates that might confound the association between air pollution and mortality. Effect estimates were determined for each city and then for the cities combined using a random effects method.

**Results:** In individual cities, associations were detected between most of the pollutants [nitrogen dioxide, sulfur dioxide, particulate matter ≤ 10 μm in aerodynamic diameter ($PM_{10}$), and ozone] and most health outcomes under study (i.e., all natural-cause, cardiovascular, and respiratory mortality). The city-combined effects of the four pollutants tended to be equal or greater than those identified in studies conducted in Western industrial nations. In addition, residents of Asian cities are likely to have higher exposures to air pollution than those in Western industrial nations because they spend more time outdoors and less time in air conditioning.

**Conclusions:** Although the social and environmental conditions may be quite different, it is reasonable to apply estimates derived from previous health effect of air pollution studies in the West to Asia.

**Key words:** air pollution, Bangkok, Hong Kong, mortality, Shanghai, time-series analysis, Wuhan. *Environ Health Perspect* 116:1195–1202 (2008). doi:10.1289/ehp.11257 available via *http://dx.doi.org/* [Online 9 July 2008]

Time-series studies of daily mortality in several Asian cities can contribute significantly to the world's literature on the health effects of air pollution. First, they provide direct evidence of air pollution effects in areas for which there are few studies. Second, because they involve different exposure conditions and populations, mortality studies of Asian cities can shed light on factors that may modify the effects of air pollution on health. In addition, multicity collaborative studies conducted within Asia, especially when analyzed using a common protocol, can generate more robust air pollution effect estimates for the region than those from individual studies and provide relevant and supportable estimates of the local impacts of environmental conditions for decision makers. Finally, they can determine the appropriateness of applying the results of health effects of air pollution studies conducted in North America and Western Europe to regions where few studies, if any, have been conducted.

Recent reviews (Anderson et al. 2004; Ostro 2004) suggest that proportional increases in daily mortality per 10-μg/m$^3$ increase in $PM_{10}$ (particulate matter ≤ 10 μm in aerodynamic diameter) are generally similar among North American and Western European regions and the few developing countries where studies have been undertaken. However, the relatively few studies that have been conducted in Asia are not geographically representative and have used different methodologies, making it difficult to compare results in Asian cities with each other or with the broader literature. In addition, the worldwide data have not been appropriately analyzed for real differences in the magnitude of the effects of short-term exposure and the possible reasons for such differences, such as sources of air pollution or population characteristics.

Efforts to bring the world's data together for such analyses are under way with funding from the Health Effects Institute (HEI) in the PAPA (Public Health and Air Pollution in Asia) project and the APHENA (Air Pollution and Health: A European and North American Approach) project. These efforts can provide important insights to the time-series literature in terms of variability in air pollution, climate, population, and city characteristics involved.

The first phase of the PAPA study was carried out using data from Bangkok, Thailand, from 1999 to 2003, Hong Kong, China, from 1996 to 2002, and Shanghai and Wuhan, China, both from 2001 to 2004 (Figure 1) (HEI 2008). A common protocol (available from the authors) for the design and analysis of data from multiple Asian cities and a management framework to conduct the coordinated analysis were established. These were designed to provide a basis for combining estimates and for isolating important independent factors that might explain effect modification in the city-specific estimates. It is anticipated that the results will not only contribute to the international scientific discussion on the conduct and interpretation of time-series studies of the health effects of air pollution but will also

Address correspondence to C.M. Wong, Department of Community Medicine, School of Public Health, The University of Hong Kong, 5/F William MW Mong Block, 21 Sassoon Road, Hong Kong China. Telephone: (852) 2819 9109. Fax: (852) 2855 9528. E-mail: hrmrwcm@hkucc.hku.hk

*Project Teams by location: Bangkok—N. Vichit-Vadakan and N. Vajanapoom (Faculty of Public Health, Thammasat University); and B. Ostro (California Environmental Protection Agency). Hong Kong—C.M. Wong, T.Q. Thach, P.Y.K. Chau, K.P. Chan, R.Y. Chung, C.Q. Ou, L. Yang, G.N. Thomas, T.H. Lam, and A.J. Hedley (Department of Community Medicine, School of Public Health, The University of Hong Kong); J.S.M. Peiris (Department of Microbiology; The University of Hong Kong); and T.W. Wong (Department of Community and Family Medicine, Chinese University of Hong Kong). Shanghai—H. Kan, B. Chen, N. Zhao, and Y. Zhang (School of Public Health, Fudan University); H. Kan and S.J. London (Epidemiology Branch, National Institute of Environmental Health Sciences); G. Song and L. Jiang (Shanghai Municipal Center of Disease Control and Prevention); G. Chen (Shanghai Environmental Monitoring Center). Wuhan—Z. Qian, H.M. Lin, C.M. Bentley (Pennsylvania State University College of Medicine); H.M. Lin (Mount Sinai School of Medicine); Q. He and L. Kong (Wuhan Academy of Environmental Science); N. Yang and D. Zhou (Wuhan Centres for Disease Prevention and Control); and S. Xu and W. Liu (Wuhan Center of Environmental Monitoring).

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stimulate the development of routine systems for recording daily deaths and hospital admissions for time-series analysis.

## Materials and Methods

***Mortality data.*** We focused on mortality from all natural causes in all ages, ≥ 65 years, and ≥ 75 years, and for cardiovascular and respiratory disease at all ages. The *International Classification of Disease, Ninth Revision* [ICD-9; World Health Organization (WHO) 1977] and *Tenth Revision* (ICD-10; WHO 1992) rubrics of the health outcomes were as follows: all natural causes, ICD-9 codes 001–799 or ICD-10 codes A00–R99; cardiovascular, ICD-9 codes 390–459 or ICD-10 codes I00–I99; and respiratory, ICD-9 codes 460–519 or ICD-10 codes J00–J98.

The sources of health data were the Ministry of Public Health, Bangkok; the Census and Statistics Department, Hong Kong; the Shanghai Municipal Center of Disease Control and Prevention, Shanghai; and the Wuhan Centre for Disease Prevention and Control, Wuhan.

***Air pollutant and meteorological data.*** Air quality indicators included nitrogen dioxide, sulfur dioxide, $PM_{10}$, and ozone. For $NO_2$, $SO_2$, and $PM_{10}$, daily data were 24-hr averages and an 8-hr average was used for $O_3$ (1000–1800 hours). Each city maintains several fixed-site air monitoring stations—dispersed throughout the metropolitan areas—that met the quality assurance and quality control procedures of local governments. The air pollutant concentrations were measured in Bangkok by the Pollution Control Department, Ministry of Natural Resources and Environment ($n$ = 10 air monitoring stations); in Hong Kong by the Environmental Protection Department ($n$ = 8); in Shanghai by the Shanghai Environmental Monitoring Center ($n$ = 6); and in Wuhan by the Wuhan Environmental Monitoring Center ($n$ = 6). The measurement methods for $NO_2$, $SO_2$, and $O_3$ were similar for the four cities based on chemiluminescence, fluorescence, and ultraviolet absorption, respectively, whereas for $PM_{10}$, the Chinese cities used tapered element oscillating microbalance and Bangkok used beta gauge monitors.

The calculation of 24-hr average concentrations of $NO_2$, $SO_2$, and $PM_{10}$, and 8-hr average concentrations of $O_3$ required at least 75% of the 1-hr values on that particular day. If > 25% of the daily values were missing for the whole period of analysis, the entire station was not included for that particular pollutant. Missing data were not imputed.

***Statistical analysis.*** The analytical methods were developed and adopted by all four teams in a common protocol. The protocol includes the specifications for selection of monitoring stations, as well as quality assurance and quality control procedures for data collection and for health outcomes and air pollutants to be included in the analysis. Generalized linear modeling was used to model daily health outcomes, with natural spline smoothers (Burnett et al. 2004; Wood 2006) for filtering out seasonal patterns and long-term trends in daily mortality, as well as temperature and relative humidity. We also included an adjustment for the day of the week and dichotomous variables relevant to individual cities if available, such as public holidays (Hong Kong) and extreme weather conditions (Wuhan). In an attempt to minimize autocorrelation, which would bias the standard errors, the aim of the core model was for partial autocorrelation function plots to have coefficients in absolute values < 0.1 for the first 2 lag days. Randomness of residuals was also considered in selecting the most appropriate models. If these criteria were not met, other methods were used to reduce autocorrelation, such as the inclusion of explanatory variables to model influenza epidemics and the addition of autoregression terms. If there were special periods with extra variations for which the core model could not account, an additional spline smoother was included. Air pollutant concentrations were entered into the core model to assess the health effects of specific pollutants. Exposure at the current day (lag 0), a 2-day average of lag 0 and lag 1 days (lag 0–1), and a 5-day average of lag 0 to lag 4 days (lag 0–4) were examined. For each pollutant, the excess risk of mortality with the 95% confidence interval (CI) per 10-μg/m$^3$ increase in average concentration at lag 0–1 was calculated. However, for brevity's sake, point estimates with $p$-values could be used to describe sets of effects.

Because several differences were observed in effect estimates among cities, we conducted additional sensitivity analyses to attempt to explain these differences and to determine the robustness of the initial findings. We focused on $PM_{10}$, given the wealth of worldwide findings of effects from this pollutant, and used the average concentration of lag 0–1 days. In these analyses we aimed to explore the impact of the following: higher concentrations of $PM_{10}$ that might be dominated by the coarse fraction and therefore have differential toxicity; monitors that might be overly affected by proximity to traffic; effects of different seasonality patterns among the cities; different controls for temperature; and different ways in aggregating daily concentration data and differences in spline


**Figure 1.** Bangkok, Hong Kong, Shanghai, and Wuhan. Numbers in parentheses indicate the number of monitoring stations used in each city.

**Table 1.** Summary statistics of daily mortality counts.

| | Mean ± SD | | | | Minimum, maximum | | | |
|---|---|---|---|---|---|---|---|---|
| | Bangkok | Hong Kong | Shanghai | Wuhan | Bangkok | Hong Kong | Shanghai | Wuhan |
| All natural causes | | | | | | | | |
| All ages | 94.8 ± 12.1 | 84.2 ± 12.8 | 119.0 ± 22.5 | 61.0 ± 15.8 | 29, 147 | 48, 135 | 51, 198 | 25, 213 |
| ≥ 65 years | 34.3 ± 6.7 | 65.4 ± 11.6 | 99.6 ± 20.6 | 43.8 ± 13.4 | 13, 63 | 34, 113 | 46, 175 | 18, 159 |
| ≥ 75 years | 21.3 ± 5.2 | 43.6 ± 9.5 | 71.5 ± 16.7 | 25.7 ± 9.5 | 6, 50 | 17, 82 | 33, 129 | 6, 106 |
| Cardiovascular | 13.4 ± 4.3 | 23.8 ± 6.5 | 44.2 ± 11.0 | 27.8 ± 8.8 | 1, 28 | 6, 54 | 11, 85 | 8, 94 |
| Respiratory | 8.1 ± 3.1 | 16.2 ± 5.2 | 14.3 ± 6.4 | 7.0 ± 5.8 | 1, 20 | 3, 34 | 3, 45 | 0, 125 |

Study period: Bangkok, 1999–2003; Hong Kong, 1996–2002; and Shanghai and Wuhan, both 2001–2004.

models. We regarded a change of excess risk > 20% from that of the analysis as an indication of sensitive results. Specifically, the sensitivity analysis included the following items:

- Exclude the daily concentration of $PM_{10}$ > 95th percentile
- Exclude the daily concentration of $PM_{10}$ > 75th percentile
- Exclude the daily concentration of $PM_{10}$ > 180 μg/m$^3$
- Exclude monitoring stations with high traffic sources (highest nitric oxide/nitrogen oxides ratio)
- Assess warm season effect with dummy variables of seasons in the core model
- Add temperature at average lag 1–2 days or 3–7 days into the model
- Use a centered daily concentration of $PM_{10}$ (Wong et al. 2001)
- Use natural spline with degrees of freedom (df) of time trend per year, temperature, and humidity fixed at 8, 4, and 4, respectively
- Use penalized spline instead of natural spline.

Combined estimates of excess risk of mortality and their standard errors were calculated using a random-effects model. Estimates were weighted by the inverse of the sum of within- and between-study variance.

Concentration–response curves for the effect of each pollutant on each mortality outcome in the four cities were plotted. We applied a natural spline smoother with 3 df on the pollutant term. We assessed nonlinearity by testing the change of deviance between a nonlinear pollutant (smoothed) model with 3 df and linear pollutant (unsmoothed) model with 1 df.

The main analyses and the combined analysis were performed using R, version 2.5.1 (R Development Core Team 2007). We also used mgcv, a package in R.

## Results

Table 1 summarizes the mortality data for the four cities, and Table 2 summarizes the pollution and meteorological variables. The daily mortality counts for all natural causes at all ages for each city showed more marked seasonal variations in the cities farther north. Shanghai (mean daily deaths, 119; population, 7.0 million) and Bangkok (95; 6.8 million) had higher daily numbers of deaths than Hong Kong (84; 6.7 million) and Wuhan (61; 4.2 million). The ratios for causes of death due to cardiovascular disease relative to respiratory disease were the highest in Wuhan (4:1) followed by Shanghai (3:1), Bangkok (2:1), and Hong Kong (1.5:1). The proportion of total cardiorespiratory mortality was also the highest in Wuhan (57%) followed by Shanghai (49%), Hong Kong (48%), and Bangkok (23%) [Table 1; Supplemental Material, Table 1 (available online at http://www.ehponline.org/members/2008/11257/suppl.pdf)]. Deaths occurring at ≥ 65 years of age were less frequent in Bangkok (36%) than in the three Chinese cities (72–84%).

As indicated in Table 2 and Figure 2, Wuhan showed the highest concentrations of $PM_{10}$ and $O_3$, whereas Shanghai had the highest concentrations of $NO_2$ and $SO_2$. The latter was probably due to the significant local contribution of power plants in Shanghai's metropolitan area. To provide an indication of the relative magnitude of the pollution concentrations in these four large Asian cities, we compared them to the 20 largest cities in the United States using data from 1987 to 1994 from the National Morbidity, Mortality, and Air Pollution Study (NMMAPS) (Samet et al. 2000). Generally, in the PAPA cities, the concentrations of $PM_{10}$ and $SO_2$ were much higher than those reported in the United States ($PM_{10}$ means of 52–142 μg/m$^3$ in the cities of the PAPA study vs. 33 μg/m$^3$ in NMMAPS, and $SO_2$ means of 13–45 μg/m$^3$ vs. 14 μg/m$^3$); comparisons of $NO_2$ and $O_3$ showed a fairly similar pattern.

We demonstrated the adequacy of the core models with partial autocorrelation function plots of the residuals in the previous 2 days, all within |0.1| [Supplemental Material, Figure 1 (available online at http://www.ehponline.org/members/2008/11257/suppl.pdf)].

In individual cities, for all natural causes at all ages (Table 3) the percentage of excess risk per 10-μg/m$^3$ associated with $NO_2$ ranged from 0.90 to 1.97 (all $p$-values ≤ 0.001); with $SO_2$, from 0.87 to 1.61 (all $p$-values ≤ 0.05); with $PM_{10}$, from 0.26 to 1.25 (all $p$-values ≤ 0.001); and with $O_3$, from 0.31 to 0.63 (all

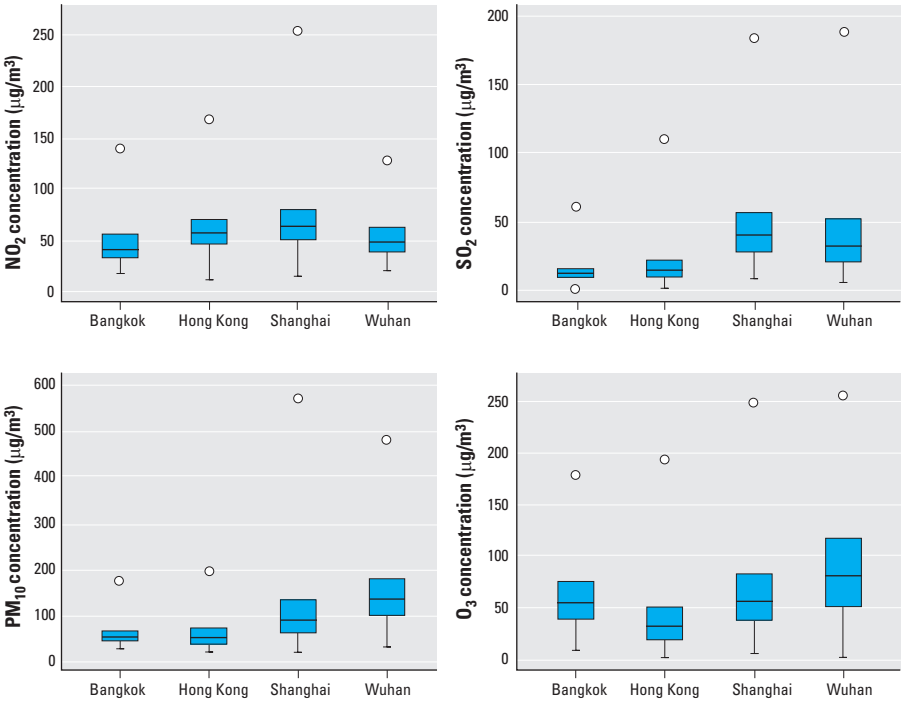


**Figure 2.** Box plots of the air pollutants for the four cities. Boxes indicate the interquartile range (25th percentile–75th percentile); lines within boxes indicate medians; whiskers and circles below boxes represent minimum values; and circles above boxes indicate maximum values.

**Table 2.** Summary statistics of air pollutant concentrations and meteorological conditions.

| | Mean | | | | Median | | | | IQR | | | | Minimum, maximum | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Bangkok | Hong Kong | Shanghai | Wuhan | Bangkok | Hong Kong | Shanghai | Wuhan | Bangkok | Hong Kong | Shanghai | Wuhan | Bangkok | Hong Kong | Shanghai | Wuhan |
| $NO_2$ (μg/m$^3$) | 44.7 | 58.7 | 66.6 | 51.8 | 39.7 | 56.4 | 62.5 | 47.2 | 23.1 | 24.4 | 29.0 | 24.0 | 15.8, 139.6 | 10.3, 167.5 | 13.6, 253.7 | 19.2, 127.4 |
| $SO_2$ (μg/m$^3$) | 13.2 | 17.8 | 44.7 | 39.2 | 12.5 | 14.7 | 40.0 | 32.5 | 5.5 | 12.6 | 28.7 | 30.8 | 1.5, 61.2 | 1.4, 109.3 | 8.4, 183.3 | 5.3, 187.8 |
| $PM_{10}$ (μg/m$^3$) | 52.0 | 51.6 | 102.0 | 141.8 | 46.8 | 45.5 | 84.0 | 130.2 | 20.9 | 34.9 | 72.0 | 80.2 | 21.3, 169.2 | 13.7, 189.0 | 14.0, 566.8 | 24.8, 477.8 |
| $O_3$ (μg/m$^3$) | 59.4 | 36.7 | 63.4 | 85.7 | 54.4 | 31.5 | 56.1 | 81.8 | 36.2 | 31.6 | 45.1 | 67.4 | 8.2, 180.6 | 0.7, 195.0 | 5.3, 251.3 | 1.0, 258.5 |
| Temperature (°C) | 28.9 | 23.7 | 17.7 | 17.9 | 29.1 | 24.7 | 18.3 | 18.5 | 1.8 | 8.0 | 14.4 | 16.3 | 18.7, 33.6 | 6.9, 33.8 | –2.4, 34.0 | –2.5, 35.8 |
| RH (%) | 72.8 | 77.9 | 72.9 | 74.0 | 73.0 | 79 | 73.5 | 74.0 | 10.8 | 10.0 | 15.5 | 19.0 | 41.0, 95.0 | 27, 97.0 | 33.0, 97.0 | 35.0, 99.0 |

Abbreviations: IQR, interquartile range; RH, relative humidity. $NO_2$, $SO_2$, and $PM_{10}$ are expressed as 24-hr averages, and $O_3$ is an 8-hr average.

*p*-values ≤ 0.05), but the effect in Wuhan was not significant. The excess risk showed trends of increasing risk with increasing age for all four pollutants. The trends for the age-specific effects were the strongest in Bangkok, less strong in Hong Kong and Wuhan, but absent in Shanghai (Figure 3). For all four pollutants, the excess risk in Bangkok was higher than those in the three Chinese cities. When the pollutant concentrations were expressed as the interquartile range (IQR; i.e., 75th percentile–25th percentile), Bangkok estimates were comparable to those of the three Chinese cities, particularly in all ages. Within cities, the effect estimates of different pollutants were also comparable to each other (data not shown).

In all cities, there was heterogeneity in effect estimates for $NO_2$ and $PM_{10}$ on all natural-cause mortality and for $PM_{10}$ on cardiovascular mortality (Table 3). For all natural-cause mortality, the combined random effects excess risk were 1.23, 1.00, 0.55, and 0.38% for $NO_2$, $SO_2$, $PM_{10}$, and $O_3$, respectively (all *p*-values ≤ 0.05). The results for cardiovascular mortality (Table 3) followed a generally similar pattern, with the highest excess risk per 10-μg/m$^3$ in Bangkok for $PM_{10}$ and $O_3$, and in Wuhan for $NO_2$ and $SO_2$. All of the cities demonstrated significant associations for each pollutant except $SO_2$ in Bangkok and $O_3$ in Wuhan, whereas all of the combined estimates were statistically significant. A similar pattern was shown for respiratory mortality, for which the highest estimates were found in Wuhan for $NO_2$ and $SO_2$ and in Bangkok for $PM_{10}$ and $O_3$. All the random effects estimates were statistically significant at the 5% level except for $O_3$.

For the lag effects in the three Chinese cities, with a few exceptions, the average lag 0–1 days usually generated the highest excess risk. However, for Bangkok the longer cumulative average of lag 0–4 days generated the highest excess risk for all of the pollutants except $SO_2$. For the combined estimates, effects at the lag 0–1 days showed the highest excess risk, except $O_3$, for which the effect at lag 0–4 days was the greatest (data not shown).

Sensitivity analyses for $PM_{10}$ showed that, in general, the results were fairly robust for various concentrations, monitors, specifications for temperature, methods of aggregating daily data, df used in the smoothers, and alternative spline models. In all cases, the effect estimates were statistically significant. In all cities, the effect estimates for $PM_{10}$ were sensitive to exclusion of the higher concentrations. For the Chinese cities, this increased the excess risk > 20% for $PM_{10}$, but in Bangkok the effect estimate decreased, with the excess risk changing from 1.25% to 0.73% per 10-μg/m$^3$ increase in average concentration of lag 0–1 days (Table 4). Examination of the warm season (which varied for each city) resulted in significant increases in effect estimates for Bangkok and Wuhan but decreases in Hong Kong and, to a lesser extent, in Shanghai (excess risk changed from 0.26% to 0.24%). Adjusting for temperature through use of longer-term cumulative averages tended to decrease the $PM_{10}$ effect.

The smoothed concentration-response (CR) relationship, between all natural-cause mortality and concentration of each pollutant, appeared to be positive. Most CR curves showed linear relationships over the IQR of the concentrations (Figure 4). At all ages, tests for nonlinearity for the entire curve showed that linearity could not be rejected at the 5% level for most of the associations between air pollution and mortality (data not shown).

## Discussion

***Review of PAPA project results.*** In the city-specific main effects for the five main health outcomes under study, there were variations in effect estimates between cities. For $NO_2$ the estimates were similar in magnitude and

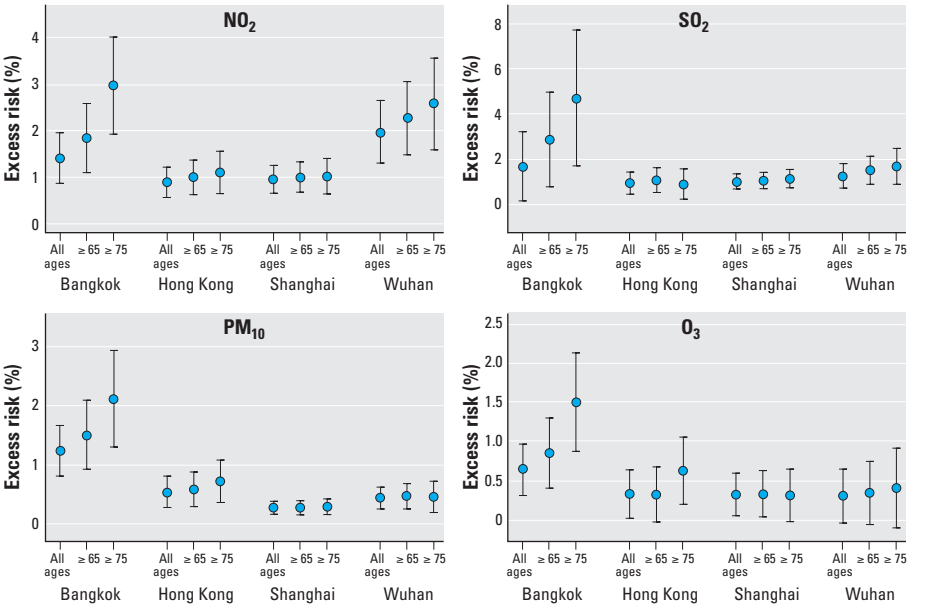


**Figure 3.** Excess risk (%) of mortality [point estimates (95% CIs)] for a 10-μg/m$^3$ increase in average concentration of lag 0–1 days for three age groups.

**Table 3.** Excess risk (ER; %) of mortality (95% CI) for a 10-μg/m$^3$ increase in the average concentration of lag 0–1 days by main effect estimates of individual cities and combined random effects.

| | | Bangkok | | Hong Kong | | Shanghai | | Wuhan | | Random effects (4 cities) | | Random effects (3 Chinese cities) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Pollutant | ER | 95% CI | ER | 95% CI | ER | 95% CI | ER | 95% CI | ER | 95% CI | ER | 95% CI |
| All natural causes (all ages) | $NO_2$ | 1.41 | 0.89 to 1.95 | 0.90 | 0.58 to 1.23 | 0.97 | 0.66 to 1.27 | 1.97 | 1.31 to 2.63 | 1.23 | 0.84 to 1.62* | 1.19 | 0.71 to 1.66* |
| | $SO_2$ | 1.61 | 0.08 to 3.16 | 0.87 | 0.38 to 1.36 | 0.95 | 0.62 to 1.28 | 1.19 | 0.65 to 1.74 | 1.00 | 0.75 to 1.24 | 0.98 | 0.74 to 1.23 |
| | $PM_{10}$ | 1.25 | 0.82 to 1.69 | 0.53 | 0.26 to 0.81 | 0.26 | 0.14 to 0.37 | 0.43 | 0.24 to 0.62 | 0.55 | 0.26 to 0.85# | 0.37 | 0.21 to 0.54 |
| | $O_3$ | 0.63 | 0.30 to 0.95 | 0.32 | 0.01 to 0.62 | 0.31 | 0.04 to 0.58 | 0.29 | –0.05 to 0.63 | 0.38 | 0.23 to 0.53 | 0.31 | 0.13 to 0.48 |
| Cardiovascular | $NO_2$ | 1.78 | 0.47 to 3.10 | 1.23 | 0.64 to 1.82 | 1.01 | 0.55 to 1.47 | 2.12 | 1.18 to 3.06 | 1.36 | 0.89 to 1.82 | 1.32 | 0.79 to 1.86 |
| | $SO_2$ | 0.77 | –2.98 to 4.67 | 1.19 | 0.29 to 2.10 | 0.91 | 0.42 to 1.41 | 1.47 | 0.70 to 2.25 | 1.09 | 0.71 to 1.47 | 1.09 | 0.72 to 1.47 |
| | $PM_{10}$ | 1.90 | 0.80 to 3.01 | 0.61 | 0.11 to 1.10 | 0.27 | 0.10 to 0.44 | 0.57 | 0.31 to 0.84 | 0.58 | 0.22 to 0.93** | 0.44 | 0.19 to 0.68 |
| | $O_3$ | 0.82 | 0.03 to 1.63 | 0.62 | 0.06 to 1.19 | 0.38 | –0.03 to 0.80 | –0.07 | –0.53 to 0.39 | 0.37 | 0.01 to 0.73 | 0.29 | –0.09 to 0.68 |
| Respiratory | $NO_2$ | 1.05 | –0.60 to 2.72 | 1.15 | 0.42 to 1.88 | 1.22 | 0.42 to 2.01 | 3.68 | 1.77 to 5.63 | 1.48 | 0.68 to 2.28 | 1.63 | 0.62 to 2.64* |
| | $SO_2$ | 1.66 | –3.09 to 6.64 | 1.28 | 0.19 to 2.39 | 1.37 | 0.51 to 2.23 | 2.11 | 0.60 to 3.65 | 1.47 | 0.85 to 2.08 | 1.46 | 0.84 to 2.08 |
| | $PM_{10}$ | 1.01 | –0.36 to 2.40 | 0.83 | 0.23 to 1.44 | 0.27 | –0.01 to 0.56 | 0.87 | 0.34 to 1.41 | 0.62 | 0.22 to 1.02 | 0.60 | 0.16 to 1.04 |
| | $O_3$ | 0.89 | –0.10 to 1.90 | 0.22 | –0.46 to 0.91 | 0.29 | –0.44 to 1.03 | 0.12 | –0.89 to 1.15 | 0.34 | –0.07 to 0.75 | 0.23 | –0.22 to 0.68 |

*p*-Values (homogeneity test): *0.01 < $p \le 0.05$; **0.001 < $p \le 0.01$; and #$p \le 0.001$.

precision for Bangkok and Wuhan, and for Hong Kong and Shanghai. The effects for Bangkok and Wuhan were higher but less precise (as reflected by a wider 95% CI) than for Shanghai and Hong Kong. For $SO_2$ the estimates for Bangkok were higher but less precise than for the three Chinese cities. For $PM_{10}$ the estimates in the three Chinese cities were very similar, but estimates were higher and less precise in Bangkok. For $O_3$ the effect estimates and the precision among the four cities were similar, although estimates in Bangkok were higher. However, when expressed by IQR increase in concentrations, the effect estimates for each pollutant were similar in the four cities.

In the combined four-city analysis, the excess risks per 10-μg/m$^3$ increase in $NO_2$ were 2–3 times greater than those derived from the APHEA (Air Pollution and Health: A European Approach) project (Samoli et al. 2006) for mortality at all ages due to all natural causes, cardiovascular disease, and respiratory disease (1.23% vs. 0.3%, 1.36% vs. 0.4%, and 1.48% vs. 0.38%, respectively). For $SO_2$, the estimate (random effects) of 1.00% for mortality due to all natural causes derived from the present study was higher than the 0.52% previously reported from the other Asian cities studied (HEI 2004) and higher than the 0.40% from the APHEA project (Katsouyani et al. 1997) [Supplemental Material, Table 2 (available online at http://www.ehponline.org/members/2008/11257/suppl.pdf)]. For $PM_{10}$, the excess risk of 0.55% for all natural causes of death at all ages was comparable to 0.49% from all Asian cities (HEI 2004), 0.5% from NMMAPS (Samet et al. 2000), and 0.6% from the APHEA project (Anderson et al. 2004). A meta-analysis of Chinese studies found that each 10-μg/m$^3$ increase in $PM_{10}$ concentration was significantly associated with 0.3% increase in all natural-cause mortality, 0.4% increase in cardiovascular mortality, and 0.6% increase in respiratory mortality (Aunan and Pan 2004). For $O_3$, the estimate from the present study was significant and higher than that from APHEA (Anderson et al. 2004) and NMMAPS (Bell et al. 2004) for all natural causes (0.38 vs. 0.20 and 0.26, respectively) and similar for cardiovascular causes (0.37 vs. 0.4 and 0.32); however, the estimates for respiratory disease (0.34 vs. –0.1 and 0.32%) were similar to those of the NMMAPS, but negative and statistically not significant ($p > 0.05$) in APHEA [Supplemental Material, Table 2).

***Review of estimates from previous Asian studies.*** For $NO_2$, we found few time-series studies, and these were mainly from South Korea (Hong et al. 1999) and Hong Kong (Wong et al. 2001). The variation of effects was large compared with other pollutants for all natural-cause mortality, respiratory mortality, and cardiovascular mortality. For $SO_2$, most time-series studies in China showed significant association with all natural-cause mortality, even at levels below the current WHO Air Quality Guideline (Chen et al. 2004; WHO 2005). A review of Asian studies (HEI 2004) also found that $SO_2$ was associated with all natural-cause mortality either from random-effects models or fixed-effects models. For $PM_{10}$, although fewer time-series studies were published from Asia than from other regions, most studies found a significant association with all natural-cause mortality, but only respiratory and cardiovascular mortality were examined in Bangkok (Ostro et al. 1999). However, significant associations with respiratory and cardiovascular mortality were not found in Seoul, Korea (Hong et al. 1999), or Hong Kong studies (Wong et al. 2001). For $O_3$ studies using different time-average concentrations such as 1, 8, and 24 hr, the estimates varied greatly between studies (HEI 2004).

In the four individual cities included in the PAPA project, consistent with other studies for Asia, air pollution effects were found in each city and for all the disease-specific outcomes under consideration. The results provide important information on air pollution–related health effects in Asia, especially for areas known to have high exposures but are underrepresented in the literature.

***Robustness of the results.*** Our sensitivity analyses indicated that most of the $PM_{10}$ effect estimates did not deviate from the main analysis > 20%. The $PM_{10}$ effect estimates were insensitive to different methods adopted, the use of higher df, and the replacement of the smoothing function by the penalized spline. However, across the four cities, additional adjustment for the average temperature at 3–7 lag days showed that the estimates for effects of $PM_{10}$ were attenuated, indicating possible residual confounding due to uncontrolled lag effects of temperature. Studies (Schwartz et al. 2004; Medina-Ramón and Schwartz 2007) show that different cumulative lag days of temperature have effects on both morbidity and mortality estimates. However, in the present study, current day temperature was specified *a priori* in the core model and was determined to be sufficient to adjust for temperature effects at the beginning of the study. On the other hand, we found high correlations between temperatures at each lag 1–7 days and at the current day, which suggest problems of multicollinearity if we make further adjustment to these lag temperature effects in the model of the main analysis.

***Scientific issues derived from PAPA study results.*** For all natural-cause, cardiovascular, and respiratory mortality, the effect estimates of $PM_{10}$ and $O_3$ are relatively similar among the three Chinese cities. However, there are some differences in the $PM_{10}$ effect estimates in that Shanghai is consistently lower, by almost half, than Hong Kong and Wuhan. These differences in effect estimates may be related to differences in the location of the monitoring stations and differences in the actual ambient levels of exposure of the population.

Estimates for $PM_{10}$ in Bangkok were higher, and the effect estimates much higher, than those of the three Chinese cities (1.25 vs. 0.26–0.53; 1.90 vs. 0.27–0.61; and 1.01 vs. 0.27–0.87). The reasons might be related to consistently higher temperature, a population that spends a longer time outdoors, and less availablity and use of air conditioning in

**Table 4.** Excess risk (ER; %) of mortality (95% CI) for a 10-μg/m$^3$ increase in the average concentration of lag 0–1 days by sensitivity analysis for $PM_{10}$ effects with variation in concentration levels, stations, seasons and methods.

| | ER | | | | Random effect (4 cities) | | | Random effect (3 Chinese cities) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| All natural causes, all ages | Bangkok | Hong Kong | Shanghai | Wuhan | ER | 95% CI | *p*-Value | ER | 95% CI | *p*-Value |
| Main analysis | 1.25 | 0.53 | 0.26 | 0.43 | 0.55 | 0.26–0.85 | # | 0.37 | 0.21–0.54 | NS |
| Omit $PM_{10}$ > 95 percentile | 0.82[a] | 0.75[a] | 0.28 | 0.52[a] | 0.53 | 0.27–0.78 | * | 0.47[a] | 0.21–0.73 | * |
| Omit $PM_{10}$ > 75 percentile | 0.73[a] | 0.89[a] | 0.36[a] | 0.70[a] | 0.53 | 0.29–0.78 | NS | 0.55[a] | 0.24–0.85 | NS |
| Omit $PM_{10}$ > 180 μg/m$^3$ | 1.25 | 0.54 | 0.22 | 0.73[a] | 0.65 | 0.24–1.06 | # | 0.46[a] | 0.15–0.76 | * |
| Omit stations with high traffic source | 1.18 | 0.54 | 0.25 | 0.45 | 0.55 | 0.26–0.85 | # | 0.38 | 0.20–0.57 | NS |
| Warm season defined by simple dichotomous variables | 2.16[a] | 0.37[a] | 0.24 | 0.81[a] | 0.86[a] | 0.11–1.60 | # | 0.43 | 0.10–0.76 | NS |
| Add temperature at lag 1–2 days | 1.06 | 0.43 | 0.23 | 0.48 | 0.51 | 0.23–0.79 | # | 0.36 | 0.18–0.53 | NS |
| Add temperature at lag 3–7 days | 0.96[a] | 0.36[a] | 0.15[a] | 0.34[a] | 0.35[a] | 0.14–0.57 | ** | 0.25[a] | 0.10–0.40 | NS |
| Daily $PM_{10}$ defined by centering | 1.20 | 0.53 | 0.26 | 0.42 | 0.54 | 0.26–0.82 | # | 0.37 | 0.21–0.53 | NS |
| Natural spline with (8, 4, 4) df | 1.23 | 0.54 | 0.28 | 0.38 | 0.54 | 0.26–0.81 | # | 0.36 | 0.23–0.49 | NS |
| Penalized spline | 1.20 | 0.48 | 0.28 | 0.39 | 0.52 | 0.26–0.77 | # | 0.34 | 0.23–0.45 | NS |

NS, not significant.
[a]ER changed > 20% from the main analysis. *p*-Values (homogeneity test): *0.01 < $p \le 0.05$; **0.001 < $p \le 0.01$; #$p \le 0.001$.

Bangkok than in the other cities (Ostro et al. 1999). With relatively higher mortality due to infectious diseases [Supplemental Material, Table 1 (available online at http://www.ehponline.org/members/2008/11257/suppl.pdf)] and with more deaths at younger ages, it is also likely that the Bangkok population is exposed to a larger number of other risk factors and may be more susceptible to the risks associated with air pollution. Tsai et al. (2000) reported that exposure levels for indoor and outdoor particulates in shopping areas were underestimated by the ambient monitoring stations in Bangkok, and therefore that the excess risk per air pollutant concentration would be higher than if it were a well-calibrated measurement. The higher ratio of $PM_{2.5}$ (PM ≤ 2.5 μm in aerodynamic diameter) to $PM_{10}$ may suggest that the proportion of smaller particles in the $PM_{10}$ composition in Bangkok is more important and might be more strongly related to adverse health effects than in the other cities (Jinsart et al. 2002).

In all the three Chinese cities, the maximum effects always occurred at lag 0–1 days, except for $O_3$ in Shanghai, where maximum effects were recorded at longer lags. The lag pattern is consistent with other reports in demonstrating a maximum at lag 1 day for most pollutants (Samoli et al. 2005, 2006). However, for $O_3$, the effect estimates are maximal at longer lags, showing that the pattern is also consistent with the literature (Goldberg et al. 2001; Wong et al. 2001). The lag patterns of $SO_2$ and $O_3$ in Bangkok are consistent with those of the three Chinese cities; however, the Bangkok lag patterns for $NO_2$ and $PM_{10}$, with greater effects at longer lags, are different from those of the three Chinese cities. For the traffic-related pollutants $NO_2$ and $PM_{10}$, the effects appear to be stronger, and they also seem to last longer in Bangkok than in the three Chinese cities.

In all cities in the PAPA study, the effects of air pollution are stronger for cardiopulmonary causes than for all natural causes. This is consistent with results from most North American and Western European studies (Anderson et al.

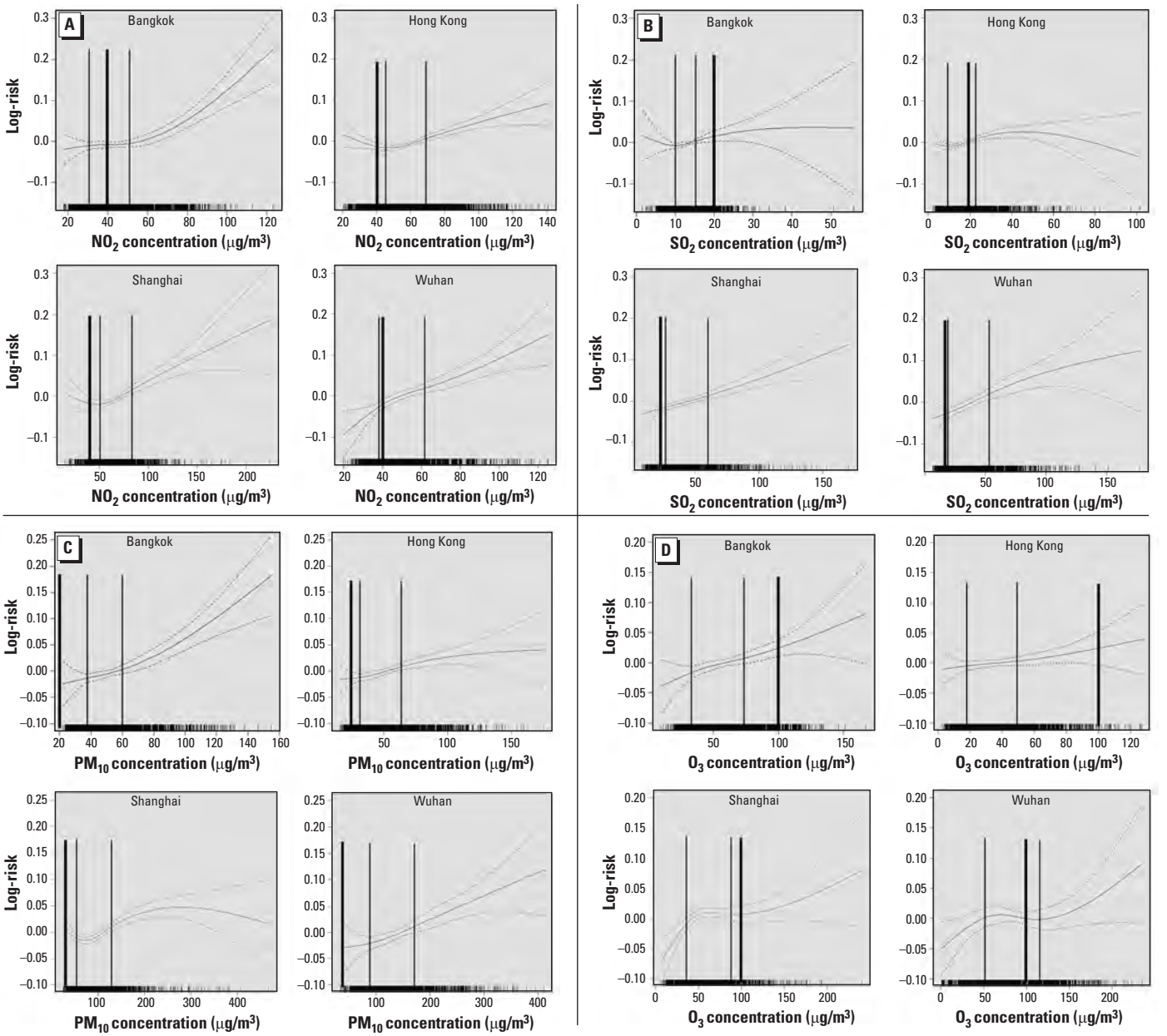


**Figure 4.** CR curves for all natural-cause mortality at all ages in all four cities for the average concentration of lag 0–1 days for $NO_2$ (*A*), $SO_2$ (*B*), $PM_{10}$ (*C*), and $O_3$ (*D*). The thin vertical lines represent the IQR of pollutant concentrations. The thick lines represent the WHO guidelines (WHO 2005) of 40 μg/m$^3$ for 1-year averaging time for $NO_2$ (*A*), 20 μg/m$^3$ for 24-hr averaging time for $SO_2$ (*B*), 20 μg/m$^3$ for 1-year averaging time for $PM_{10}$ (*C*), and 100 μg/m$^3$ for daily maximum 8-hr mean for $O_3$ (*D*).

2004; Samet et al. 2000) and supports the validity of the estimates from the present study. In addition, the effects of the four single pollutants appear to be stronger at older ages than at younger ages, particularly in Bangkok, which may have a more susceptible population than the three Chinese cities. The stronger effects at older ages for these pollutants support the validity of our estimates.

As expected, the exclusion of high levels of $PM_{10}$ concentrations from the analysis affects the effect estimates. In the present study, consistent with the literature from North America and Western Europe, exclusion of $PM_{10}$ concentrations greater than the 75th or 95th percentile produces larger estimates in all three Chinese cities. These results suggest that the CR curves might be curvilinear, with the slope less steep at higher concentrations. We cannot explain the opposite findings noted in Bangkok; however, they may be related to the exclusion of readings from one monitor located in a region with both high particulate levels and a fairly susceptible population.

The health effects estimates during the warm season are higher than those with all seasons combined in both Bangkok (excess risk 2.16 vs. 1.25%) and Wuhan (0.81 vs. 0.43%), but those in Hong Kong (0.37 vs. 0.53%) and Shanghai (0.24 vs. 0.26%) were similar or lower. These observations support the hypothesis that the populations in Bangkok and Wuhan, which are less affluent than the other two cities, may be more exposed and susceptible because of less use of air conditioning in summer; this may also explain the generally higher air pollution effects observed in Bangkok and Wuhan than in the other two cities (Long et al. 2007). The lower effect in Hong Kong may also be explained by air mass movements and southerly winds prevalent in the summer. In Wuhan the higher effect may be due to extremely high temperatures in summer. There may also be synergistic effects between $PM_{10}$ and extremely high temperatures on mortality. Nevertheless, further study will be important in understanding how results derived from hotter climates could be extrapolated to cooler climates.

Understanding the shapes of the CR curves is important for environmental public health policy decision making and setting of air quality standards. Comparison across geographic regions is also important in demonstrating causality and how effects estimated from one location can be generalized to others. The CR curves for $PM_{10}$ effects on all natural-cause mortality derived from the present study clearly show that the relationship is linear without a threshold in most of the cities studied, although some nonlinear relationships appear in Shanghai. Thus our estimates are consistent with a linear model without threshold, a finding in most North American and Western European studies (Daniels et al. 2000; Pope and Dockery 2006; Samoli et al. 2005). The CR relation of a pollutant would be affected by the method used, the susceptibility of the population being investigated, the toxicity of the pollutant, and the weather and social conditions with which the pollutant may interact.

In the present study, effect estimates for $PM_{10}$ are comparable, whereas those for gaseous pollutants, particularly for $NO_2$, are higher than those in the West. One postulation for the higher effect estimates may be related to their correlation with particulate pollutant [correlation between $PM_{10}$ and $NO_2$ ranging from 0.71 to 0.85; Supplemental Material, Table 3 (available online at http://www.ehponline.org/members/2008/11257/suppl.pdf)]. However for the three Chinese cities, the estimates for effects of $NO_2$ remain robust after adjustment for $PM_{10}$ (Supplemental Material, Figure 2A); whereas those of the $PM_{10}$ effects were attenuated (Supplemental Material, Figure 2B). But for Bangkok, the change in effect estimates for the two pollutants after adjustment for the other as a copollutant are opposite of those for the three Chinese cities. Thus in Asian cities, the observed effects of gaseous pollutants may not necessarily be related to their covariation with a particulate pollutant. Further research is needed to clarify the effects of copollutants.

***Limitations.*** Among the major limitations of our study was the difference in monitoring locations among the cities. In densely populated cities such as Hong Kong and Shanghai, the monitors tend to be close to major roadways, whereas in Bangkok and Wuhan the monitors are located farther from major pollutant sources. Thus, it is difficult to determine the true effects and to compare our results both within the PAPA cities and with previous studies. In addition, the specific components of particulate responsible for the observed health effects have not been elucidated. Such identification will aid in targeting and prioritizing future pollution control efforts. Also, information about potential effect modifiers (e.g., time spent outdoors, use of air conditioning, residential distance to roadways, housing construction, comorbidity in the population) varied in its availability and quality among the cities, making it difficult to explain quantitative differences among the PAPA cities.

## Conclusion

Effects of particulate pollutants in Asian cities are similar to or greater than those observed in most North American and Western European cities in spite of large differences in concentrations; similarly, effects of gaseous pollutants in Asian cities are as high or higher. The methodology adopted and developed in the PAPA study could be used for other countries preparing to conduct air pollution studies. In addition, results from PAPA studies can be used in Asian and other cities for health impact assessment. Finally, further efforts are needed to understand the socioeconomic and demographic factors that might modify the effects of air pollution.

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