Published in final edited form as:
Environ Res. 2010 April ; 110(3): 258–264. doi:10.1016/j.envres.2010.01.006.

Short-term association between sulfur dioxide and daily mortality: the Public Health and Air Pollution in Asia (PAPA) study

Haidong Kan[a,*], **Chit-Ming Wong**[b], **Nuntavarn Vichit-Vadakan**[c], **Zhengmin Qian**[d,e], and **the PAPA Project Teams**[†]

[a] School of Public Health, Fudan University, Shanghai, China [b] Department of Community Medicine, School of Public Health, The University of Hong Kong, Hong Kong Special Administrative Region, China [c] Faculty of Public Health, Thammasat University, Pathumthani, Thailand [d] Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA [e] Geisinger Center for Health Research, Danville, Pennsylvania, USA

Abstract

Sulfur dioxide (SO_2) has been associated with increased mortality and morbidity, but few studies were conducted in Asian countries. Previous studies suggest that SO_2 may have adverse health effects independent of other pollutants. In the Public Health and Air Pollution in Asia (PAPA) project, the short-term associations between ambient sulfur dioxide (SO_2) and daily mortality were examined in Bangkok, Thailand, and three Chinese cities: Hong Kong, Shanghai, and Wuhan. Poisson regression models incorporating natural spline smoothing functions were used to adjust for seasonality and other time-varying covariates. Effect estimates were obtained for each city and then for the cities combined. The impact of alternative model specifications, such as lag structure of pollutants and degree of freedom (df) for time trend, on the estimated effects of SO_2 were also examined. In both individual-city and combined analysis, significant effects of SO_2 on total non-accidental and cardiopulmonary mortality were observed. An increase of 10 $\mu g/m^3$ of 2-day moving average concentrations of SO_2 corresponded to 1.00% [95% confidence interval (CI), 0.75-1.24], 1.09% (95% CI, 0.71-1.47), and 1.47% (95% CI, 0.85-2.08) increase of total, cardiovascular and respiratory mortality, respectively, in the combined analysis. Sensitivity analyses suggested that these findings were generally insensitive to alternative model specifications. After adjustment for PM_{10} or O_3, the effect of SO_2 remained significant in three Chinese cities. However, adjustment for NO_2 diminished the associations and rendered them statistically insignificant in all four cities. In conclusion, ambient SO_2 concentration was associated with daily mortality in these four Asian cities. These associations may be attributable to

[*] Corresponding address: Haidong Kan, Box 249, 130 Dong-An Road, Shanghai 200032, China. haidongkan@gmail.com; telephone: +86 (21) 5423 7908; fax: +86 (21) 6404 6351..
[†]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); 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).

The authors declare they have no competing financial interests.

SO_2 serving as a surrogate of other substances. Our findings suggest that the role of outdoor exposure to SO_2 should be investigated further in this region.

Keywords

air pollution; mortality; sulfur dioxide; time-series

1. INTRODUCTION

Ambient air pollution is a complex mixture composed of both suspended particulates and gaseous pollutants. Identification of specific pollutants contributing most to the health hazard of air pollution mixture may have important implications for environmental and social policies, and for local government in taking steps to protect the human health. Although the strongest evidence linking outdoor air pollutants with adverse health effects thus far is for solid particulates (Dockery, 2009), many researchers have reported associations for gaseous pollutants such as nitrogen dioxide (NO_2) (Burnett et al., 2004; Samoli et al., 2006), ozone (O_3) (Bell and Dominici, 2008; Bell et al., 2004), and sulfur dioxide (SO_2) (Stieb et al., 2002; Stieb et al., 2003). Recent multi-city analyses conducted in Europe provide further evidence supporting the short-term association of SO_2 with adverse health endpoints including both mortality (Katsouyanni et al., 1997) and morbidity (Sunyer et al., 2003a; Sunyer et al., 2003b). SO_2 is a respiratory irritant and bronchoconstrictor, and has been associated with cardiovascular abnormalities including decrease in heart rate variability (Tunnicliffe et al. 2001), providing a mechanism by which SO_2 affects cardiorespiratory health. However, recent findings about the independent health effect of SO_2 remain inconsistent. For example, after adjusting for PM_{10} (i.e. particles with size <10 μm), Sunyer et al (Sunyer et al., 2003b) reported associations of ambient SO_2 with cardiovascular admissions, particularly for ischemic heart diseases, in seven European cities; however, the SO_2 association with respiratory admission disappeared after adjustment for PM_{10} in the same cities (Sunyer et al., 2003a). Also, to our knowledge, there have been no multi-city studies of SO_2 in the Asian region.

In Asian developing countries, the characteristics of outdoor air pollution (e.g. air pollution level, chemical composition and size of particles, and fate and transport of pollutants), meteorological conditions and socio-demographic patterns are different from North America and Western Europe. However, there have been only a limited number of air pollution health studies conducted in this region (Health Effects Institute, 2004). Because of the wide use of high sulfur fuel (e.g. coal) and inefficient technology in removal of sulfur, the ambient SO_2 levels in Asian countries are much higher than in developed countries (Guttikunda et al., 2003). The objective of this paper is to examine the short-term associations between SO_2 and daily mortality in four Asia cities – Bangkok (BK), Thailand; Hong Kong (HK), China; Shanghai (SH), China; and Wuhan (WH), China. This study is a component of the joint *Public Health and Air Pollution in Asia* (PAPA) program supported by the Health Effects Institute (HEI) (Kan et al., 2008; Wong et al., 2008).

2. MATERIALS AND METHODS

2.1 Data

The study periods were 1999–2003 for Bangkok, 1996–2002 for Hong Kong, and 2001–2004 for both Shanghai and Wuhan. The sources of mortality 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. The causes of death were coded according to

International Classification of Diseases, Revision 9 (ICD-9) or 10 (ICD-10). The mortality data were classified into deaths due to total non-accidental causes (ICD-9 <800; ICD-10 A00-R99), cardiovascular disease (ICD-9 390-459; ICD-10 I00-I99), and respiratory disease (ICD-9 460-519; ICD-10 J00-J98).

The sources of air pollutant concentrations were the Pollution Control Department, Ministry of Natural Resources and Environment, Bangkok (10 air monitoring stations); the Environmental Protection Department, Hong Kong (8 stations); the Shanghai Environmental Monitoring Center, Shanghai (6 stations); and the Wuhan Environmental Monitoring Center, Wuhan (6 stations). Air quality indicators included SO_2, particulate matter with aerodynamic diameter of 10 micrometers or less (PM_{10}), nitrogen dioxide (NO_2), and ozone (O_3). 24-hour average concentrations for SO_2, PM_{10}, NO_2, and maximal 8-hour mean concentrations for O_3 were collected. For the calculation of 24-hour mean concentrations of PM_{10}, SO_2 and NO_2, as well as maximal 8-hour mean O_3 concentrations, at least 75% of the one-hour values must be available on that particular day. If a station had more than 25% of the values missing for the whole period of analysis, the entire station was excluded from the analysis. In each city, the location of monitoring stations were not in the direct vicinity of traffic or of industrial sources, and were mandated not to be influenced by local pollution sources and should also avoid buildings, or housing large emitters such as coal-, waste-, or oil-burning boilers, furnaces, and incinerators. Thus the monitoring results should reflect the general background urban air pollution level rather than local sources such as traffic or industrial combustion.

To allow adjustment for the effect of weather on mortality, meteorological data (daily mean temperature and humidity) were obtained at each city.

All the death, air pollution and meteorological data were validated by an independent auditing team assigned by the HEI. The team checked samples of the original death certificates and monitoring records, and validated the generation progress of death, air pollution and weather data used for the statistical analysis in each city. The data quality was assured to be satisfactory and thus the differences in measurement errors may be minimal.

2.2 Statistical analysis

The single-city analytical method was developed and commonly adopted by the four teams in a common protocol which comprises a communication network between the four teams and the Health Effects Institute International Scientific Oversight Committee (ISOC), specification for selection of monitoring stations, quality assurance or quality control for the data collection, health outcomes and air pollutants to be included in the analysis (Wong et al., 2008). The protocol also developed the methods to standardize data management including compilation of daily data. The methods were tailor made to suit the local situation, including the specifications for selection of monitoring stations and quality assurance and quality control procedures for data collection on 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. The partial autocorrelation function (PACF) was used to guide the selection of degree of freedom (*df*) for time trend in the core models. When the absolute magnitude of the PACF plot was less than 0.1 for the first two lag days, the core models were regarded as adequate. If this criterion was not met, other methods were used to reduce autocorrelation, such as the inclusion of explanatory variables to model influenza epidemics and the addition of auto-regression terms. If there were special periods with extra variations for which the core model could not account, an additional spline smoother would be included. Also, 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), was included. Residuals of the core models were examined to check whether there were discernable patterns and autocorrelation by means of residual plots and PFACF plots.

SO_2 concentrations were entered into the core model to assess its health effects in each city. Combined estimates of SO_2 on daily mortality were calculated using a fixed- or random-effects model. Estimates were weighted by the inverse of the sum of within- and between-study variance. Homogeneity tests were performed by means of Chi-square tests for the differences in sum of squares between individual and weighted average of the estimates.

Because the assumption of the linearity between the log of mortality and SO_2 may not be justified, the smoothing function with 3 *df* was used to graphically describe their relationships. Test of non-linearity was assessed by testing the change of deviance between a non-linear pollutant (smoothed) model with 3 df and linear pollutant (unsmoothed) model with 1 df.

Single-day lag models were reported to underestimate the cumulative effect of air pollution on mortality (Dockery, 2009); therefore, 2-day moving average of current and previous day concentrations (lag 01) were used in our main analyses. As a sensitivity analysis, the effects of SO_2 with different lag structures, including current day (lag 0) and five-day average of lags 0 to 4 (lag 04), were also examined.

Given that it is not easy to determine the optimal values of df for time trend, sensitivity analyses were conducted to test the impact of alternative df values on the estimated effect of SO_2. Also, both single- and multi-pollutant models were fitted to assess the stability of SO_2 effect estimate; up to two pollutants were included per model.

All analyses were conducted in R 2.5.1 using the MGCV package (R Development Core Team, 2007). Cross-checking of results between teams was performed by pairing up the teams; Hong Kong was assigned to pair with Wuhan, and Bangkok was assigned to pair with Shanghai.

3. RESULTS

Table 1 summarizes the mortality and air pollution data in the four cities. In our research periods (1999-2003 for Bangkok, 1996-2002 for Hong Kong, and 2001-2004 for both Shanghai and Wuhan), the mean daily death numbers for all non-accidental causes, cardiovascular causes and respiratory causes were 94.8, 13.4 and 8.1, respectively, for Bangkok; 84.2, 23.8, and 16.2 for Hong Kong; 119.0, 44.2 and 14.3 for Shanghai; and 61.0, 27.8, and 7.0 for Wuhan (Table 1). Among all deaths, cardiorespiratory causes accounted for 23% in Bangkok, 48% in Hong Kong, 49% in Shanghai, and 57% in Wuhan. The concentrations of SO_2 were similar in Bangkok and Hong Kong, and were lower than both Shanghai and Wuhan (Table 1). The relatively higher levels of SO_2 in Shanghai (mean: 44.7 $\mu g/m^3$) and Wuhan (mean: 39.2 $\mu g/m^3$) might be due to the significant local contribution of power plants in the two cities. Bangkok (mean: 13.2 $\mu g/m^3$) and Hong Kong (mean: 17.8 $\mu g/m^3$) had levels that were less than half of those of Wuhan and Shanghai. The SO_2 levels in the two Mainland Chinese cities were 2-3 times higher than in European cities (Sunyer et al., 2003a; Sunyer et al., 2003b). SO_2 had much higher correlation coefficients with PM_{10} and NO_2 in Shanghai and Wuhan than in Bangkok and Hong Kong (Table 2). In all four cites, SO_2 was weakly correlated with O_3.

We found significant associations between SO_2 levels and daily mortality from all causes and from cardiorespiratory diseases in each of the four cities (Table 3). An increase of 10 $\mu g/m^3$ of 2-day moving average concentrations of SO_2 corresponds to 1.61% [95%

confidence interval (CI), 0.08-3.16], 0.87% (95%CI, 0.38-1.36), 0.95% (95%CI, 0.62-1.28), and 1.19% (95%CI, 0.65-1.74) increase of total non-accidental mortality in Bangkok, Hong Kong, Shanghai, and Wuhan, respectively. SO_2 had significant associations with cardiovascular and respiratory mortality only in three Chinese cities, but not in Bangkok.

In the four-city combined analysis, there was no significant heterogeneity for the associations of SO_2 with either total or cardiopulmonary mortality. An increase of 10 $\mu g/m^3$ of 2-day moving average concentrations of SO_2 corresponded to 1.00% (95%CI, 0.75-1.24), 1.09% (95%CI, 0.71-1.47), and 1.47% (95%CI, 0.85-2.08) increase of total, cardiovascular and respiratory mortality, respectively (Table 3).

There were positive concentration-response relationships between total mortality and SO_2 level in all four cities (Figure 1). For Shanghai and Wuhan, an almost linear relationship was found. For Bangkok and Hong Kong, the relationship seemed to be J-shaped or U-shaped nonlinear for most of the SO_2 levels, although tests for non-linearity were significant only in Hong Kong ($p < 0.05$). Lack of data at high SO_2 concentrations may contribute to the inverted U-shaped and wider confidence interval in the concentration-response curve of Hong Kong.

The results for the effects of alternative lags on all-cause mortality are summarized in Figure 2. For three Chinese cities, with a few exceptions, the lag 0-1 usually generated the highest effect estimates of SO_2. However, for Bangkok, the effects of SO_2 were similar using different lag structures. For the combined-analysis results, the lag 0-1 showed the highest effect estimates.

Within the range of 4-12, the change of df/yr for time trend does not substantially affect the estimated effects of SO_2 (Figure 3), suggesting that our findings are relatively robust in this aspect.

In the three Chinese cities, the associations of SO_2 with total and cardiopulmonary mortality were only minimally altered by adding PM_{10} and O_3 into the models (Figure 4). However, adjustment for NO_2 decreased the associations and rendered them statistically insignificant in these Chinese cities. In Bangkok, the effects of SO_2 decreased and became statistically insignificant after adjustment for any co-pollutants.

For the results of the cross-checking, no discrepancies were found between the original estimates and the estimates obtained in the cross-checking assessment.

4. DISCUSSION

This combined analysis summarizes the results from four Asian cities concerning the short-term effects of SO_2 on daily mortality. Significant associations of SO_2 with total and cardiopulmonary mortality were found, and these findings were generally insensitive to alternative model specifications. To our knowledge, this is the first multi-city analysis in Asia to report the acute health effect of SO_2. Our findings are consistent with previous results of SO_2 in the APHEA (Air Pollution and Health: a European Approach) (Katsouyanni et al., 1997) and APHEA-2 studies (Sunyer et al., 2003a; Sunyer et al., 2003b), although the estimated effect of SO_2 on daily mortality in these four Asian cities were moderately larger than those found in other locations (Katsouyanni et al., 1997; Stieb et al., 2002; Stieb et al., 2003). Lower proportion of cardiorespiratory deaths might contribute to the uncertain results for Bangkok (Table 3).

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 SO_2 and PM_{10} were much higher than those reported in the United States (SO_2 means of 13-45 $\mu g/m^3$ in the cities of the PAPA study vs. 14 $\mu g/m^3$ in NMMAPS, and PM_{10} means of 52-142 $\mu g/m^3$ vs. 33 $\mu g/m^3$); comparisons of NO_2 and O_3 showed a fairly similar pattern.

There were similarities as well as dissimilarities in effect estimates of SO_2 between these four cities. The estimates for Bangkok were relatively higher but less precise as compared with the three Chinese cities. The lack of precision in the Bangkok estimates may be due to a lack of variability in SO_2 (the SD of SO_2 in BK is 4.8 $\mu g/m^3$ compared with 12.1–25.3 $\mu g/m^3$ in the Chinese cities). When the effects were expressed per inter-quartile range increase, the estimates were very similar in the four cities (data not shown).

We did observe non-linear relationships between SO_2 and mortality risk in Bangkok and Hong Kong, although for most SO_2 concentrations, the concentration-response (C-R) relationship still appeared to be positive, and with concentration below 50 $\mu g/m^3$ the concentration-response curve was similar to that in Bangkok. Higher effect estimates at lower concentration levels for SO_2 has also been reported from a Germany study (Wichmann et al., 2000). In this respect, one might postulate, with support from the biological mechanism, that scrubbing effects of the upper airway in response to SO_2 may be stronger at a higher concentration than at lower concentration for the pollutant (Schlesinger, 1999). We could not ignore that a non-linear relationship between SO_2 and mortality may be operating in some population and environment, e.g. Hong Kong. The C-R relation of a pollutant would be affected by the method being used, the susceptibility of the population being investigated, the toxicity nature of the pollutant, as well as the weather and social conditions under which the pollutant may be interacted. Therefore the C-R relationships are subject to substantial uncertainty especially for those above the third quartile of air pollutant concentration. Further research is needed in these aspects.

After adjusting for PM_{10} or O_3, the association of SO_2 remained significant in three Chinese studies (Figure 3), suggesting that SO_2 is important for the air pollution mixture in China. Previously, the health effects of SO_2 were extensively reported in China. In Beijing, for example, Xu and coworkers found that it was SO_2, not total suspended particle (TSP), that was associated with daily mortality (Xu et al., 1994) and morbidity (Xu et al., 1995). In Chongqing, Venners et al found that SO_2 had significant effects on daily mortality even after adjustment for $PM_{2.5}$, while the effect of $PM_{2.5}$ diminished after adjustment for SO_2 (Venners et al., 2003). Also in Hong Kong, the strongest effects of outdoor air pollution were found for gases including SO_2 rather than PM_{10} (Wong et al., 2001). The most convincing evidence of the independent health effects of SO_2 thus far is from an intervention study in Hong Kong which showed SO_2 resulting from sulfur-rich fuels had an direct impact on cardiorespiratory deaths (Hedley et al., 2002). Outside of China, similar independent effects of SO_2 were presented in a European multi-city analysis (Katsouyanni et al., 1997; Sunyer et al., 2003a; Sunyer et al., 2003b). In Bangkok, the effect of SO_2 became insignificant after adjustment for PM_{10} or O_3. The discrepancy between the effects of SO_2 in Bangkok and three Chinese cities might be caused by differences in the characteristics of local air pollution or patterns of exposure among local residents.

The effect estimate for SO_2 decreased and became insignificant after adjustment for NO_2 in all four cities (Figure 4); however, SO_2 or other pollutants (PM_{10} and O_3) did not confound the effect of NO_2 (data not shown). The fact that NO_2 reduces the association of SO_2 with daily mortality in our study may be because both pollutants probably come from the same source (i.e. fossil fuel combustion or diesel exhaust) or may increase together due to the

meteorological conditions. SO_2 may serve as a surrogate of other substances also correlated with NO_2.

The biological mechanism by which exposure to SO_2 may increase mortality is not well understood but has received considerable attention. SO_2 is a known respiratory irritant and bronchoconstrictor, but its effects seem limited to patients with asthma and bronchitis, although sensitivity to exposure varies widely (Nowak et al., 1997). Previous study found a change in heart rate variability in humans associated with exposure to SO_2 (200 ppb for 1 h) (Tunnicliffe et al., 2001), providing a mechanism which may be operating in the SO_2 mortality associations. SO_2 can be converted to sulfuric acid, which then can be carried into the small airways by inhalable particulates and impair lung function in children (Spengler et al., 1996). SO_2 also contribute to particle formation; Zhang et al found that concentration of SO^{2-}_4 in the air was closely associated with chronic disease mortality in Beijing (Zhang et al., 2000).

Most air pollution epidemiologic studies, including ours, use ambient pollutant concentrations as surrogates of personal exposure. Given the correlations between SO_2 and co-pollutants in the urban air, it is difficult to disentangle the specific effect of each pollutant. The observed health effects attributed to SO_2 might actually be a result of exposures to fine particles or traffic-related emissions (Sarnat et al., 2005; Sarnat et al., 2001). Actually some authors have suggested that the pollutants measured and included in models of daily mortality might be better interpreted as indicators of the biologically relevant pollutant mixture and that the best indicators might vary in different geographic areas (Sarnat et al., 2001). To our knowledge, there have been no studies in Asian examining the associations between ambient SO_2 concentrations, personal exposure to SO_2 and personal PM exposure. We therefore can not conclude that SO_2 is a proxy of fine particle or the components of fine particle, or SO_2 has a direct short-term effect on mortality.

Our analysis has strengths and limitations. These four Asian cities offer advantages for the study of the air pollution-mortality relationship in that they are generally very densely populated. As in most previous time-series studies, we simply averaged the monitoring results across various stations as the proxy for population exposure level to air pollution. The simple averaging method may raise a number of issues given that pollutant measurements can differ from monitoring location to monitoring location and that ambient monitoring results differ from personal exposure level to air pollutants (Sarnat et al., 2005). Numerous factors, such as air conditioning and ventilation rate between indoor and outdoor air, may affect the monitoring results from fixed stations as surrogates of personal exposure to air pollutants (Janssen et al., 2002). Because we were unable to measure the true population exposures in these four cities, we could not determine the direction of the bias and its impact on our conclusions.

In summary, we found significant associations of ambient SO_2 concentrations with daily mortality in these four Asian cities. These associations were generally independent of PM_{10} and O_3 but did not persist after adjustment for NO_2. Our findings suggest that the role of outdoor exposure to SO_2, especially the ambient-personal associations, should be investigated further in this region.

Acknowledgments

Research described in this article was conducted under contract to the Health Effects Institute (HEI), an organization jointly funded by the U.S. Environmental Protection Agency (EPA; Assistance Agreement R82811201) and automobile manufacturers. The contents of this article do not necessarily reflect the views of HEI, nor do they necessarily reflect the views and policies of the U.S. EPA or of motor vehicle and engine manufacturers. Haidong Kan was supported by the Gong-Yi Program of China Ministry of Environmental

Protection (200809109), National Natural Science Foundation of China (30800892), and Shanghai Pu Jiang Program (09PJ1401700).

This study does not involve experimental animals or individual information of human subjects. The protocols of this study were approved by the Institutional Review Board of each Institution.

Abbreviations

$\mu g/m^3$	micrograms per cubic meter
95% CI	95 percent confidence interval
df	degree of freedom
DOW	day of the week
GAM	generalized additive model
ICD-9	the 9^{th} revision of International Classification of Diseases
ICD-10	the 10^{th} revision of International Classification of Diseases
NO_2	nitrogen dioxide
O_3	ozone
PM_{10}	particulate matter less than 10 microns in diameter
SO_2	sulfur dioxide

REFERENCE

Bell ML, Dominici F. Effect modification by community characteristics on the short-term effects of ozone exposure and mortality in 98 US communities. Am J Epidemiol. 2008; 167:986–97. [PubMed: 18303005]

Bell ML, et al. Ozone and short-term mortality in 95 US urban communities, 1987-2000. Jama. 2004; 292:2372–8. [PubMed: 15547165]

Burnett RT, et al. Associations between short-term changes in nitrogen dioxide and mortality in Canadian cities. Arch Environ Health. 2004; 59:228–36. [PubMed: 16201668]

Dockery DW. Health effects of particulate air pollution. Ann Epidemiol. 2009; 19:257–63. [PubMed: 19344865]

Guttikunda SK, et al. The contribution of megacities to regional sulfur pollution in Asia. Atmos Environ. 2003; 37:11–22.

Health Effects Institute. Health effects of outdoor air pollution in developing countries of Asia: a literature review. Boston, MA, USA: 2004.

Hedley AJ, et al. Cardiorespiratory and all-cause mortality after restrictions on sulphur content of fuel in Hong Kong: an intervention study. Lancet. 2002; 360:1646–52. [PubMed: 12457788]

Janssen NA, et al. Air conditioning and source-specific particles as modifiers of the effect of PM(10) on hospital admissions for heart and lung disease. Environ Health Perspect. 2002; 110:43–9. [PubMed: 11781164]

Kan H, et al. 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. Environ Health Perspect. 2008; 116:1183–8. [PubMed: 18795161]

Katsouyanni K, et al. Short-term effects of ambient sulphur dioxide and particulate matter on mortality in 12 European cities: results from time series data from the APHEA project. Air Pollution and Health: a European Approach. Bmj. 1997; 314:1658–63. [PubMed: 9180068]

Nowak D, et al. Airway responsiveness to sulfur dioxide in an adult population sample. Am J Respir Crit Care Med. 1997; 156:1151–6. [PubMed: 9351615]

R Development Core Team. R: A Language and Environment for Statistical Computing, version 2.5.1. R Foundation for Statistical Computing; Vienna: 2007.

Samet JM, et al. Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994. N Engl J Med. 2000; 343:1742–9. [PubMed: 11114312]

Samoli E, et al. Short-term effects of nitrogen dioxide on mortality: an analysis within the APHEA project. Eur Respir J. 2006; 27:1129–38. [PubMed: 16540496]

Sarnat JA, et al. Ambient gas concentrations and personal particulate matter exposures: implications for studying the health effects of particles. Epidemiology. 2005; 16:385–95. [PubMed: 15824556]

Sarnat JA, et al. Gaseous pollutants in particulate matter epidemiology: confounders or surrogates? Environ Health Perspect. 2001; 109:1053–61. [PubMed: 11675271]

Schlesinger, RB. Toxicology of sulfur oxides. Holgate, ST., et al., editors. Air pollution and health; 1999. p. 585-602.

Spengler JD, et al. Health effects of acid aerosols on North American children: air pollution exposures. Environ Health Perspect. 1996; 104:492–499. [PubMed: 8743436]

Stieb DM, et al. Meta-analysis of time-series studies of air pollution and mortality: effects of gases and particles and the influence of cause of death, age, and season. J Air Waste Manag Assoc. 2002; 52:470–84. [PubMed: 12002192]

Stieb DM, et al. Meta-analysis of time-series studies of air pollution and mortality: update in relation to the use of generalized additive models. J Air Waste Manag Assoc. 2003; 53:258–61. [PubMed: 12661685]

Sunyer J, et al. Respiratory effects of sulphur dioxide: a hierarchical multicity analysis in the APHEA 2 study. Occup Environ Med. 2003a; 60:e2. [PubMed: 12883029]

Sunyer J, et al. The association of daily sulfur dioxide air pollution levels with hospital admissions for cardiovascular diseases in Europe (The Aphea-II study). Eur Heart J. 2003b; 24:752–60. [PubMed: 12713769]

Tunnicliffe WS, et al. The effect of sulphur dioxide exposure on indices of heart rate variability in normal and asthmatic adults. Eur Respir J. 2001; 17:604–8. [PubMed: 11401052]

Venners SA, et al. Particulate matter, sulfur dioxide, and daily mortality in Chongqing, China. Environ Health Perspect. 2003; 111:562–7. [PubMed: 12676616]

Wichmann HE, et al. Daily mortality and fine and ultrafine particles in Erfurt, Germany part I: role of particle number and particle mass. Res Rep Health Eff Inst. 2000:5–86. discussion 87-94. [PubMed: 11918089]

Wong CM, et al. Effect of air pollution on daily mortality in Hong Kong. Environ Health Perspect. 2001; 109:335–340. [PubMed: 11335180]

Wong CM, et al. Public Health and Air Pollution in Asia (PAPA): a multicity study of short-term effects of air pollution on mortality. Environ Health Perspect. 2008; 116:1195–202. [PubMed: 18795163]

Wood, SN. Generalized Additive Models: An Introduction with R. Chapman & Hall/CRC; Boca Raton, FL: 2006.

Xu X, et al. Association of air pollution with hospital outpatient visits in Beijing. Arch Environ Health. 1995; 50:214–220. [PubMed: 7618954]

Xu X, et al. Air pollution and daily mortality in residential areas of Beijing. China. Arch Environ Health. 1994; 49:216–22.

Zhang J, et al. Ambient sulfate concentration and chronic disease mortality in Beijing. Sci Total Environ. 2000; 262:63–71. [PubMed: 11059843]

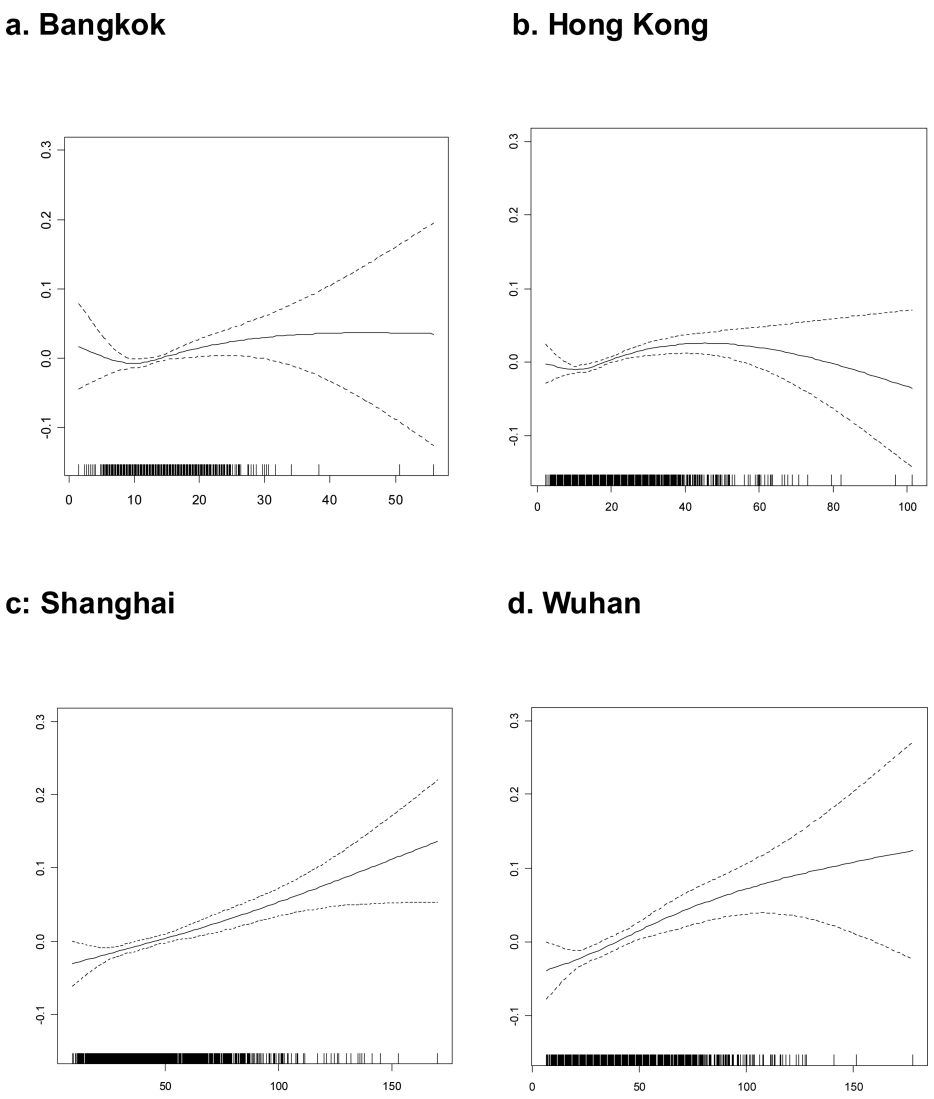

Figure 1.

Smoothing plots of SO_2 against total mortality risk (df = 3) in each city. X-axis is the 2-day average (lag01) SO_2 concentrations ($\mu g/m^3$). The solid lines indicate the estimated mean percentage of change in daily mortality, and the dotted lines represent twice the standard error

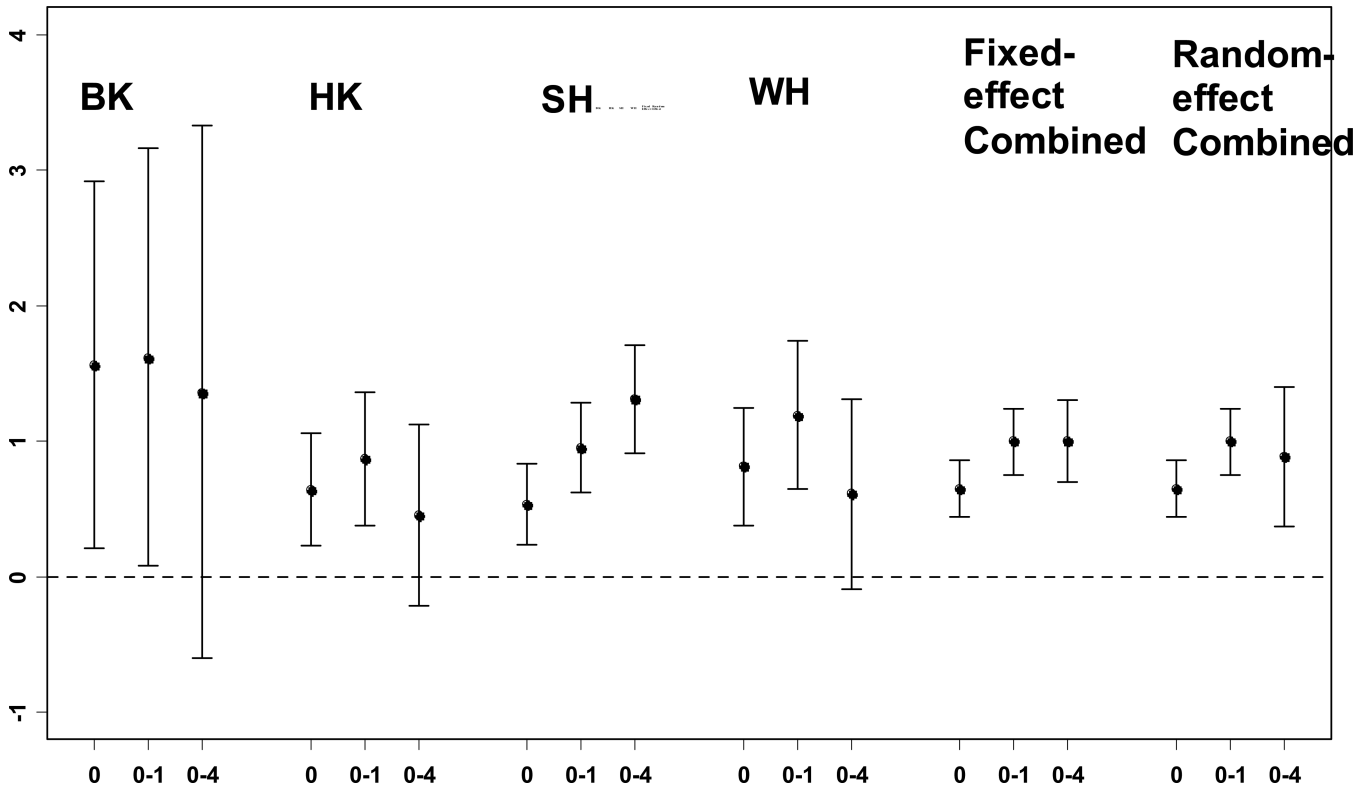

Figure 2.

Percent increase of total mortality associated with 10 μg/m^3 increase of SO_2, using different lag structures (lag0, lag01, and lag 04) – individual and combined effects. X-axis is lag structures. Y-axis is percent increase of total mortality.

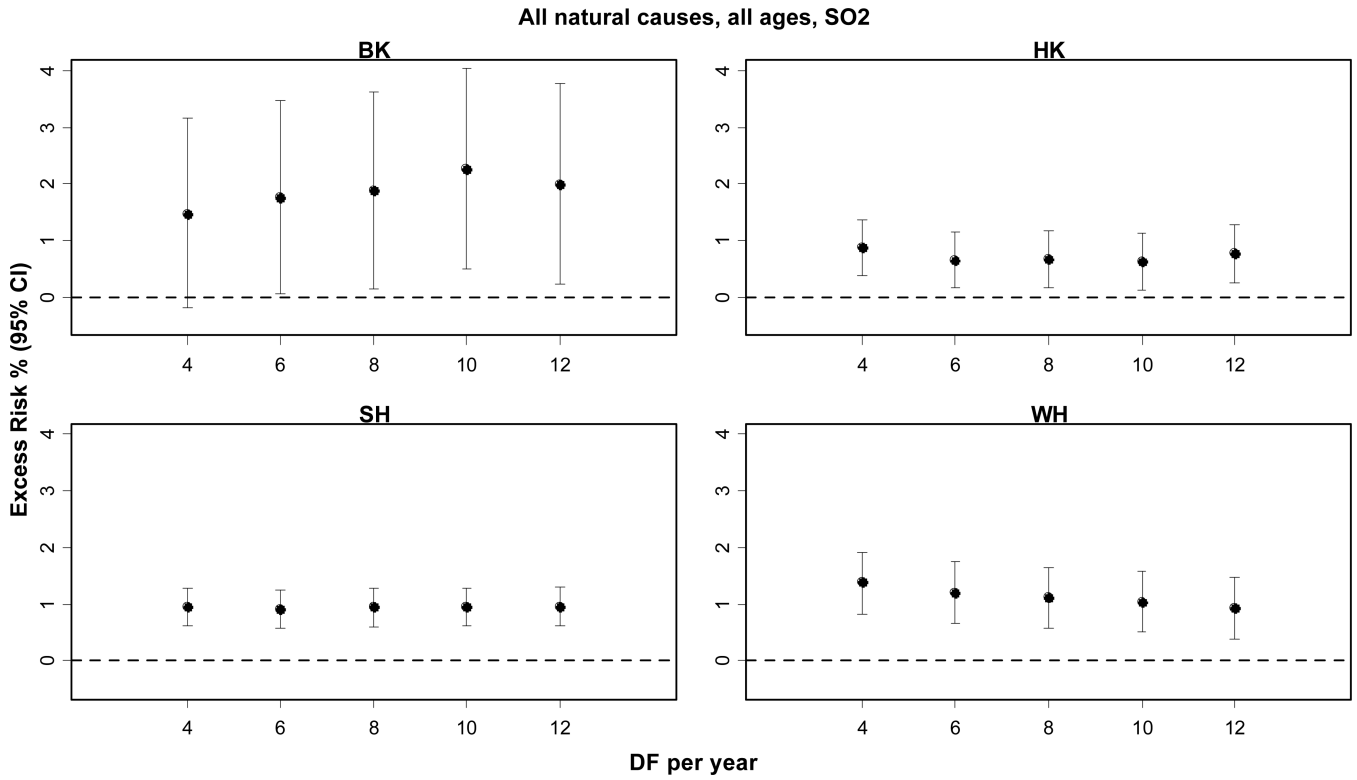

Figure 3.
Percent increase of total mortality associated with 10 μg/m^3 increase of 2-day moving average SO_2, using different df/yr for time trend

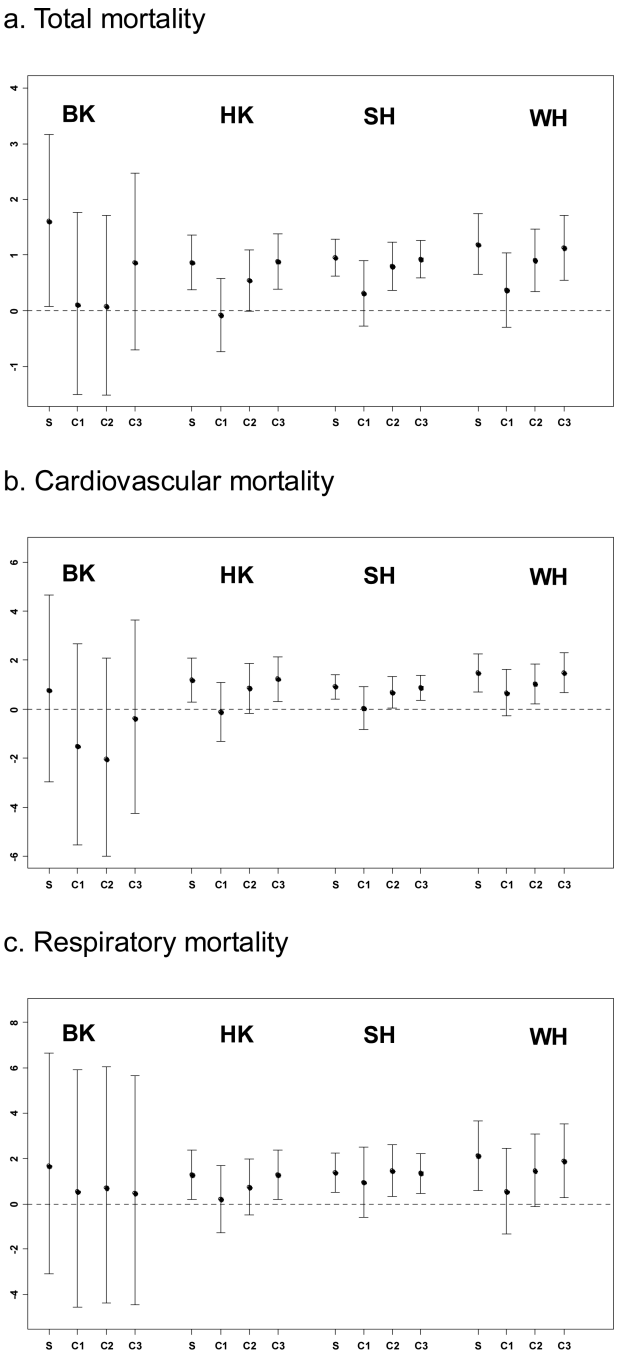

Figure 4.

Percent increase of mortality outcomes associated with 10 μg/m^3 increase of 2-day moving average SO_2 with single and two-pollutant models [a] [a] S: sing-pollutant model; C1: two-pollutant model (SO_2 + NO_2); C2: two-pollutant model (SO_2 + PM_{10}); C3: two-pollutant model (SO_2 + O_3)

Table 1

Mean (and standard deviation) of daily mortality counts and air pollutant concentrations per city

	Total mortality (no.)	Cardiovascular mortality (no.)	Respiratory mortality (no.)	SO_2 (μg/m^3)[a]	PM_{10} (μg/m^3)[a]	NO_2 (μg/m^3)[a]	O_3 (μg/m^3)[a]
Bangkok (1999-2003)	94.8 (12.1)	13.4 (4.3)	8.1 (3.1)	13.2 (4.8)	52.0 (20.1)	44.7 (17.3)	59.4 (26.4)
Hong Kong (1996-2002)	84.2 (12.8)	23.8 (6.5)	16.2 (5.2)	17.8 (12.1)	51.6 (25.3)	58.7 (20.1)	36.7 (22.9)
Shanghai (2001-2004)	119.0 (22.5)	44.2 (11.0)	14.3 (6.4)	44.7 (24.2)	102.0 (64.8)	66.6 (24.9)	63.4 (36.7)
Wuhan (2001-2004)	61.0 (15.8)	27.8 (8.8)	7.0 (5.8)	39.2 (25.3)	141.8 (63.7)	51.8 (18.8)	85.7 (47)

[a]Multi-year mean (and standard deviation) of pollutant concentrations.

Table 2

Pearson correlation coefficients of SO_2 with co-pollutants in the four cities[a]

	Bangkok	Hong Kong	Shanghai	Wuhan
NO_2	0.27	0.37	0.64	0.76
PM_{10}	0.24	0.24	0.67	0.65
O_3	0.18	-0.13	0.19	0.09

[a] $p < 0.001$ for all coefficients.

Table 3

Excess risk (ER; %) of daily mortality associated with 10 μg/m^3 increase of 2-day moving average SO_2 concentrations – effect estimates of individual cities and combined effects

	Bangkok	Hong Kong	Shanghai	Wuhan	Random effect[a] (4 cities)
	ER 95% CI	ER 95% CI	ER 95% CI	ER 95% CI	ER 95% CI
Total	1.61 (0.08, 3.16)	0.87 (0.38, 1.36)	0.95 (0.62, 1.28)	1.19 (0.65, 1.74)	1.00 (0.75, 1.24)
Cardiovascular	0.77 (-2.98, 4.67)	1.19 (0.29, 2.10)	0.91 (0.42, 1.41)	1.47 (0.70, 2.25)	1.09 (0.71, 1.47)
Respiratory	1.66 (-3.09, 6.64)	1.28 (0.19, 2.39)	1.37 (0.51, 2.23)	2.11 (0.60, 3.65)	1.47 (0.85, 2.08)

[a]Because of the lack of heterogeneity, the fixed and random effects are identical.

Environ Res. Author manuscript; available in PMC 2012 July 10.