Particulate Matter, Sulfur Dioxide, and Daily Mortality in Chongqing, China

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In 1995, daily mortality in a district of Chongqing, China, was analyzed from January through December for associations with daily ambient sulfur dioxide and fine particles (airborne particles with diameters ≤ 2.5 μm; $PM_{2.5}$). The mean concentration of $PM_{2.5}$ was 147 μg/m^3 (maximum, 666 μg/m^3), and that of SO_2 was 213 μg/m^3 (maximum, 571 μg/m^3). On average, 9.6 persons died each day. We used a generalized additive model using robust Poisson regression to estimate the associations of mean daily SO_2 and $PM_{2.5}$ with daily mortality (on the same day and at lags up to 5 days) adjusted for trend, season, temperature, humidity, and day of the week. The relative risk of mortality associated with a 100 μg/m^3 increase in mean daily SO_2 was highest on the second lag day [1.04; 95% confidence interval (CI), 1.00–1.09] and the third lag day (1.04; 95% CI, 0.99–1.08). The associations between daily mortality and mean daily $PM_{2.5}$ were negative and statistically insignificant on all days. The relative risk of respiratory mortality on the second day after a 100 μg/m^3 increase in mean daily SO_2 was 1.11 (95% CI, 1.02–1.22), and that for cardiovascular mortality was 1.10 (95% CI, 1.02–1.20). The relative risk of cardiovascular mortality on the third day after a 100 μg/m^3 increase in mean daily SO_2 was 1.20 (95% CI, 1.11–1.30). The relative risks of mortality due to cancer and other causes were insignificant on both days. The estimated effects of mean daily SO_2 on cardiovascular and respiratory mortality risk remained after controlling for $PM_{2.5}$. *Key words:* China, daily mortality, particulate matter, sulfur dioxide. *Environ Health Perspect* 111:562–567 (2003). doi:10.1289/ehp.5664 available via *http://dx.doi.org/* [Online 30 October 2002]

Studies using time-series analyses have been conducted in a number of cities worldwide to investigate the association between daily changes in ambient air pollution and population risk of daily mortality (Hales et al. 2000; Lee et al. 1999; Stieb et al. 2002; Touloumi et al. 1996; Zmirou et al. 1996). Although many studies have found that particulate matter (PM) was independently associated with mortality (Samet et al. 2000; Schwartz 1994), they have less consistently found an independent association between sulfur dioxide and mortality. In some studies, SO_2 was not significantly associated with mortality after adjustment for particulates (Schwartz and Dockery 1992), but other studies have reported positive associations between daily SO_2 and mortality risk that remained even after adjustment for particulates (HEI 2000; Katsouyanni et al. 1997; Lee et al. 2000). Epidemiologic studies from different locations in China have consistently demonstrated significant positive associations of SO_2 with increased morbidity (Wang et al. 1997; Xu et al. 1995a, 1995b, 1995c) and mortality (Dong et al. 1995; Gao et al. 1993; Xu et al. 1994) even after adjustment for total suspended particulates (TSPs). The discrepancy between the consistency of SO_2 results found in studies conducted in China compared with those conducted outside of China might be caused by real differences in the characteristics of Chinese air pollution or patterns of exposure among Chinese citizens. However, recent refinements in investigations of PM suggest the possibility that associations between SO_2 and mortality in Chinese studies might have been confounded. Recent reports suggest that fine particulates of aerodynamic diameters of ≤ 2.5 μm ($PM_{2.5}$) might be a better measure of the causal component of particulates responsible for increased mortality (Klemm et al. 2000; Schwartz et al. 1996) than are TSPs or particulates of aerodynamic diameters of ≤ 10 μm (PM_{10}). Because previous studies in China did not control for $PM_{2.5}$, it is not clear whether the associations between SO_2 and health outcomes found in these studies were confounded by unmeasured $PM_{2.5}$.

A collaborative epidemiologic investigation was conducted in 1995 in the Shi-Zhong District of Chongqing, China, to measure ambient air pollution and to assess its health effects. In this report, we present the association of $PM_{2.5}$ and SO_2 with daily mortality.

Materials and Methods

Study area. Chongqing is the largest city in China, with a population of more than 30 million. Located on the Yangtze River, it has five urban districts and 43 rural counties. We conducted our investigation in Shi-Zhong District, an urban district of 18 km^2 with a population of 576,000 people and located in the middle of Chongqing that has served as a national mortality-monitoring site since the early 1980s. Shi-Zhong District is a center of commercial administration, finance, and information and a central hub for both water and ground transportation. Many heavy industries, including power plants and several large steel and iron smelters, were located in Chongqing at the time of this study. Because the city was surrounded by mountains, air pollution in urban Chongqing often reached high levels. The coal being used there had high sulfur content (ranging from 4% to 12%) and had long been the dominant energy source both in households and industry. Previous monitoring data from the local environmental institute showed that the annual average level of air pollution did not differ greatly among various districts in urban Chongqing.

Air pollution and weather. We measured $PM_{2.5}$ and SO_2 daily throughout 1995 at two Shi-Zhong District sites. $PM_{2.5}$ monitoring was performed for 7 months, and SO_2 was monitored for the entire year. The samples were collected in 24-hr periods at two roadside sites chosen to represent areas of differing principal social activities. One site was located in the center of the downtown area, along a commercial street on which there was a high level of vehicular traffic. The other site was located just outside the downtown area along a street in a residential area. Five duplicate samples per month were collected at each site to verify data quality. Rigorously trained personnel carried out the sampling protocols. During implementation of the study, videotapes of sampling procedures in the field were made at each site

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and reviewed by expert technicians to verify the quality of the sampling procedures. The methods for sampling and weighing $PM_{2.5}$ were identical to those in the Harvard Six Cities Study and have been described previously (Dockery et al. 1993). All filters were pre- and postweighed at the Environmental Science and Engineering Program, Harvard School of Public Health. We monitored SO_2 using an SO_2 bubbler (AGL, North Sydney, Australia) and the acid titration method (BSI British Standards 1991). The mean values of SO_2 and $PM_{2.5}$ from the two monitoring sites were used for all analyses. Temperature and humidity data were obtained from the Chongqing Weather Bureau.

Daily mortality. Shi-Zhong District daily mortality data for calendar year 1995 were obtained from death certificates recorded at the Chongqing Anti-Epidemic Station, located in Shi-Zhong District. In the event of a death in Chongqing, the family of the deceased was required to obtain a death certificate from the hospital or local community clinic. This certificate was submitted to the police station to cancel the household registration of the deceased and to the local Anti-Epidemic Station to have the home of the deceased "sterilized" according to health law.

Deaths were first coded in the Chinese Classification of Causes of Disease (CCD; ZRFHDMRM 1987) and then transcribed into the *International Classification of Disease, Revision 9* (ICD-9; WHO 1984) (Dong and Ding 1992). Deaths caused by accidents (CCD, E1–E15; ICD-9, > 800) were excluded, as were all deaths that occurred outside the city. Total mortality was subdivided by cause of death: cardiovascular disease (CCD, 42, 44–47, 49–51; ICD-9, 390–414, 417–448), respiratory causes (CCD, 54; ICD-9, 490–493), cancer (CCD, 22; ICD-9, 140–208), and other causes.

Data analysis. We first generated a core model using robust Poisson regression with allowance for overdispersion (Hastie and Tibshirani 1990) to control for gradual time trends due to environmental or population changes, periodic seasonal trends, meteorologic factors, and day-of-the-week effects. We added terms stepwise beginning with trend and season followed by temperature, humidity, and day of the week. Using cross-validation (Hastie and Tibshirani 1990) and analysis of residuals, we selected a cubic smoothing spline of time to model long-term and seasonal trends. Using cross-validation, we added the best-fitting single terms for both temperature and humidity after testing the fit of cubic smoothing splines of values on the same day and at lags up to 3 days previous. We modeled day-of-the-week effects after testing the significance of linear terms for each day and analyzing the autocorrelation function of the model residuals to identify the best fit.

We investigated the effects of SO_2 and $PM_{2.5}$ on total daily mortality using linear terms for these pollutants added to our robust Poisson model of trend, season, weather, and day-of-the-week effects. We first modeled SO_2 individually and tested its effects on deaths occurring on the same day and at lags up to 5 days. We then repeated this analysis for $PM_{2.5}$ excluding those days for which there were no $PM_{2.5}$ measurements. Using our SO_2 models, we tested the effects of controlling for $PM_{2.5}$ on the same day as mortality and on each day before mortality up to 5 days. These models were first analyzed using data from all days after setting missing values of $PM_{2.5}$ equal to 0 and including a variable in our models having a value of 1 when $PM_{2.5}$ measurements were missing and a value of 0 otherwise. Second, they were analyzed using only data from days that had both SO_2 and $PM_{2.5}$ measurements. All analyses were repeated for each specific cause of mortality (respiratory, cardiovascular, cancer, or other) after repeating the core model-building process for each.

We conducted two additional tests of the robustness of our results. First, a potential limitation of our study was partial ascertainment of mortality because of death reports being filed with the Anti-Epidemic Station several months after the actual time of death. Therefore, some deaths that occurred in late 1995 might not have been reported until 1996 and would therefore not have been included in our data. One indication of this was a gradual downward trend in the daily numbers of reported deaths that was evident in the second half of 1995. We also found that some deaths that occurred in late 1994 had not been reported until early 1995, further supporting the likelihood that the downward trend in daily mortality counts in the latter half of 1995 derived from late reporting of deaths. Because late reporting of deaths would not have been associated with air pollution levels on or shortly before the time of death, and because our models included a cubic smoothing spline of time to control for long-term trends, our results were unlikely to be biased by partial ascertainment of mortality. Nevertheless, we repeated our analyses using only the data from the first 6 months of 1995 when we expected there would be fewer missing reports. Second, when we observed a graphic representation of the residuals of our core model by day (which included terms for long-term and seasonal trends, temperature, humidity, and day-of-the-week effects), we found 3 days with atypically large residuals. The numbers of deaths on these 3 days were

Table 1. Summary statistics for mortality, weather variables, and pollution concentrations.

	No. of observations	Minimum	Mean	Maximum
Mortality (count)				
Total	365	0	9.6	47
Respiratory	365	0	2.1	20
Cardiovascular	365	0	2.9	17
Cancer	365	0	0.4	3
Other	365	0	4.2	18
Air pollutants				
SO_2 (μg/m^3)	365	32.0	213.0	571.0
$PM_{2.5}$ (μg/m^3)	213	44.7	146.8	666.2
Weather				
Temperature (°C)	365	5.1	18.5	35.7
Humidity (%)	365	47	80	98

Table 2. Estimated effects of 100 μg/m^3 changes in SO_2 and $PM_{2.5}$[a] on daily total mortality risk.

Mortality lag (days)	Coefficient[b]	Standard error	*t*-Value	Relative risk (95% CI)
SO_2				
0	0.009	0.023	0.41	1.01 (0.96–1.06)
1	0.029	0.023	1.27	1.03 (0.98–1.08)
2	0.043	0.023	1.90	1.04 (1.00–1.09)
3	0.035	0.023	1.51	1.04 (0.99–1.08)
4	0.008	0.023	0.34	1.01 (0.96–1.05)
5	0.012	0.023	0.53	1.01 (0.97–1.06)
$PM_{2.5}$				
0	–0.001	0.034	–0.04	1.00 (0.93–1.07)
1	–0.023	0.035	–0.65	0.98 (0.91–1.04)
2	–0.003	0.035	–0.10	1.00 (0.93–1.07)
3	–0.040	0.034	–1.19	0.96 (0.90–1.03)
4	–0.034	0.034	–1.02	0.97 (0.90–1.03)
5	–0.007	0.034	–0.20	0.99 (0.93–1.06)

[a]SO_2 and $PM_{2.5}$ modeled singly; available data: SO_2, 365 days; $PM_{2.5}$, 213 days. [b]Coefficient representing ln(relative risk) estimated using robust Poisson regression with allowance for overdispersion and adjustment for trend, season, weather, and day of the week.

38, 42, and 47, whereas death counts on the remaining days of the year ranged from 0 to 24. Because the counts from these peak mortality days might have overly influenced our parameter estimates, we reanalyzed our data after excluding the 3 days with extremely high mortality counts. We simultaneously excluded pollution concentrations on each of these days and the 5 days before each.

Results

Using cross-validation (Hastie and Tibshirani 1990) and analysis of residuals, we selected a cubic smoothing spline of time with 4 degrees of freedom to model long-term and seasonal trends. Analysis of the model residuals showed that the single term captured the effects of both trend and season. Using cross-validation, we added a term each for temperature and humidity after testing the fit of cubic smoothing splines of values on the same day and at lags up to 3 days previous. Our final model included smoothing splines with 4 degrees of freedom for temperature on the same day and humidity on the day before. We modeled day-of-the-week effects after testing the significance of linear terms for each day and analyzing the autocorrelation function of the model residuals. Because Saturday and Sunday were the only significantly different days and the effects on these days were similar, we included a single term for weekend in our final model.

Table 1 shows the distribution of air pollution, weather, and daily mortality during the study period. $PM_{2.5}$ concentrations (mean, 147 μg/m^3; maximum, 666 μg/m^3) and SO_2 concentrations (mean, 213 μg/m^3; maximum, 571 μg/m^3) were both high. An average of 9.6 persons died each day. Cardiovascular disease was recorded as the cause in 30% of deaths, cancer in 4%, and respiratory disease in 22%. Measured $PM_{2.5}$ and SO_2 had a correlation coefficient of 0.45 on the days with observations of both pollutants.

Because high air pollution episodes often occurred for several consecutive days and because air pollution might have had a delayed effect, our models predicted both current and day-lagged, all-cause mortality from daily air pollution measurements (Table 2). The regression coefficients for increased risk of mortality due to increased SO_2 were positive at all lags and highest on the second and third lag days, whereas coefficients for $PM_{2.5}$ were all negative and statistically insignificant.

We evaluated the independent associations of SO_2 and $PM_{2.5}$ with cause-specific mortality: cardiovascular, respiratory, cancer, and others. No significant associations were found between $PM_{2.5}$ and any cause of mortality. Significant positive associations were observed between increased SO_2 and cardiovascular mortality on the second and third lag days and between SO_2 and respiratory mortality on the second lag day (Figure 1).

Table 3 shows the estimated effect of a 100 μg/m^3 increase in mean SO_2 concentrations on total and cause-specific mortality on the second and third lag days. The relative risk on the second lag day for respiratory mortality was 1.11 [95% confidence interval (CI), 1.02–1.22], and that for cardiovascular mortality was 1.10 (95% CI, 1.02–1.20). The relative risk of cardiovascular mortality on the third lag day was 1.20 (95% CI, 1.11–1.30). The relative risks of mortality due to cancer and other causes were not statistically significant on any days. When we tested the robustness of the SO_2 associations with mortality risk observed on lag days 2 and 3 by adding linear terms for $PM_{2.5}$ (on the same day as mortality and up to 5 days before) to our models, all parameter estimates for SO_2 remained stable. Table 4 shows the estimated effects of a 100 μg/m^3 increase in SO_2 on respiratory mortality on the second lag day and cardiovascular mortality on the third lag day when modeled simultaneously with terms for $PM_{2.5}$ increases on the same day and up to 5 days previous.

We performed two tests of robustness on the estimated effects of daily ambient SO_2 on total and cause-specific mortality on the second and third lag days (Table 5). The analyses were first repeated using data from January–June to test the effect of possible partial ascertainment of mortality counts in the later months. We then tested for influential data points using the January–December data by excluding counts on three unusually

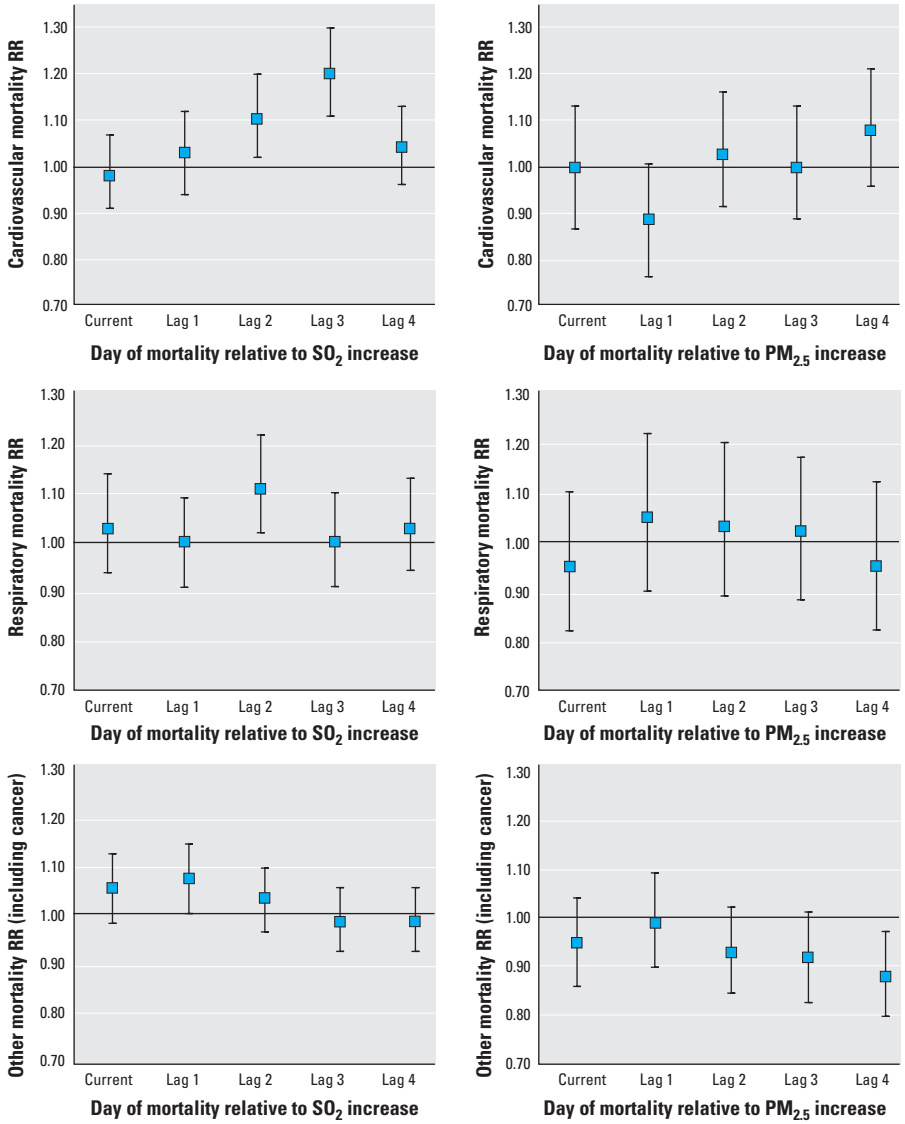

Figure 1. Estimated effects of 100 μg/m^3 changes in SO_2 and $PM_{2.5}$ on relative risks (RR) of cardiovascular, respiratory, and other (including cancer) mortality on the same day and at lags up to 4 days. Error bars show 95% CI.

high-mortality days and pollution data on each high-mortality day and the 5 days before it. Table 5 shows the results of the original analysis and two robustness analyses. When the data were restricted to the first 6 months, the estimated relative risk of cardiovascular mortality due to SO_2 increased on the second lag day, whereas all other associations remained within the 95% CIs of the original analysis. When high-mortality days and associated pollution levels were excluded, the estimated effects of SO_2 on respiratory and cardiovascular mortality were decreased and became statistically insignificant on the second lag day. However, the association seen with cardiovascular mortality on the third lag day was unchanged.

Discussion

This study was conducted in the Shi-Zhong District of Chongqing, China, and demonstrated positive associations between daily ambient SO_2 concentrations and population risk of mortality, especially that from respiratory or cardiovascular causes. We did not observe an association between daily ambient $PM_{2.5}$ concentrations and any cause of mortality. The associations found between daily ambient SO_2 and mortality were unchanged when we controlled for $PM_{2.5}$ in our models.

This population provided several advantages compared with those of previous studies. Shi-Zhong District of Chongqing, China, was very densely populated. Therefore, this population was unique in the proximity of a large number of people to ambient samplers. Most patients sought health care within their district because there were many good hospitals and clinics there. In addition, because few hospital wards or homes in Chongqing were equipped with air conditioning, windows were kept open most of the time from March to November. Thus, monitored ambient air pollution data might have been more highly associated with average population exposures in Chongqing than in other study locations.

Our estimates of the effects of SO_2 on daily mortality were similar to those of previous studies that found independent associations between SO_2 and mortality risk after controlling for PM. A meta-analysis of results from Western European cities found 50 μg/m^3 increases of SO_2 associated with pooled relative risks of 1.04 (95% CI, 1.01–1.06) for deaths from cardiovascular conditions and 1.05 (95% CI, 1.03–1.07) for respiratory conditions (Zmirou et al. 1998). A report from Lyon, France, showed 50 μg/m^3 increases of SO_2 associated with relative risks of 1.54 (95% CI, 1.22–1.96) for deaths from cardiovascular conditions and 1.22 (95% CI, 1.05–1.40) from respiratory conditions (Zmirou et al. 1996). Consistent with our results, some previous studies were unable to demonstrate an association between particulates and mortality (or found the particulate association was no longer significant after controlling for SO_2) (Lee et al. 2000; Moolgavkar 2000). However, our results differ from several reports of associations between daily mortality risk and $PM_{2.5}$ (Borja-Aburto et al. 1998; Fairley 1999; Schwartz et al. 1996).

Several studies have included pollutants other than particulates and SO_2 in models of daily mortality, including carbon monoxide, carbon dioxide, nitrogen dioxide, and ozone. A recent comprehensive meta-analysis of 109 daily time-series studies of air pollution and mortality concluded that PM_{10}, CO, NO_2, O_3, and SO_2 were all positively and significantly associated with all-cause mortality (Stieb et al. 2002). In an analysis of daily nonaccidental mortality and the urban ambient air pollution mixtures from 1980 to 1991 in 11 Canadian cities, Burnett et al. (1998a) found that NO_2, O_3, SO_2, and CO were all significantly and positively associated with daily mortality in a model simultaneously including all four pollutants (but no measure of PM). Moolgavkar (2000) conducted a time-series analysis of total daily deaths and those specifically due to cardiovascular, cerebrovascular, and chronic obstructive pulmonary disease in three major metropolitan areas, including measures of PM_{10}, CO, SO_2, NO_2, and O_3 and in one area also $PM_{2.5}$. He found considerable heterogeneity between cities in the pollutants associated with mortality. In general,

Table 3. Estimated effects of 100 μg/m^3 increase in daily SO_2 concentrations on total and cause-specific mortality on the second and third lag days.

Cause of mortality	RR (95% CI) of mortality[a]	
	Second lag day[b]	Third lag day[b]
Total	1.04 (1.00–1.09)	1.04 (0.99–1.08)
Respiratory	1.11 (1.02–1.22)*	1.00 (0.91–1.10)
Cardiovascular	1.10 (1.02–1.20)*	1.20 (1.11–1.30)**
Cancer	1.02 (0.79–1.02)	0.94 (0.74–1.18)
Other	1.03 (0.97–1.10)	0.99 (0.93–1.06)

[a]Relative risk (RR) estimated using robust Poisson regression with allowance for overdispersion and adjustment for trend, season, weather, and day of the week. [b]Following an increase of 100 μg/m^3 in daily mean SO_2. *$p < 0.05$; **$p < 0.001$.

Table 4. Robustness of SO_2 effect estimates when controlling for $PM_{2.5}$ in models of relative risks of respiratory and cardiovascular mortality due to increased SO_2.

Day of $PM_{2.5}$ modeled[a]	RR (95% CI) due to increased SO_2[b]	
	Respiratory mortality on the second lag day	Cardiovascular mortality on the third lag day
Same day	1.12 (1.02–1.23)*	1.21 (1.11–1.30)**
1 day before	1.13 (1.03–1.24)*	1.20 (1.11–1.29)**
2 days before	1.14 (1.04–1.26)*	1.20 (1.11–1.30)**
3 days before	1.13 (1.03–1.23)*	1.22 (1.12–1.32)**
4 days before	1.12 (1.02–1.23)*	1.18 (1.09–1.28)**
5 days before	1.11 (1.01–1.21)*	1.19 (1.09–1.28)**

[a]Single, linear term for $PM_{2.5}$ concentration added to model. [b]Relative risk (RR) due to an increase of 100 μg/m^3 in daily mean SO_2 estimated using robust Poisson regression with allowance for overdispersion and adjustment for trend, season, weather, day of week, missing $PM_{2.5}$ values, and indicated lag of $PM_{2.5}$. *$p < 0.05$; **$p < 0.001$.

Table 5. Estimated relative risks of total and cause-specific mortality at lags of 2 and 3 days associated with 100 μg/m^3 increases in SO_2 concentrations using data from full year, first 6 months, and full year excluding high-mortality days.

Mortality	(January–December)	Six months (January–June)	Excluding high-mortality days[a] (January–December)
RR (95% CI) of mortality on lag day 2 with increased SO_2[b]			
Total	1.04 (1.00–1.09)	1.08 (1.02–1.14)	1.02 (0.97–1.07)
Respiratory	1.11 (1.02–1.22)*	1.16 (1.04–1.29)*	1.07 (0.98–1.18)
Cardiovascular	1.10 (1.02–1.20)*	1.23 (1.11–1.17)*	1.05 (0.96–1.14)
Cancer	1.02 (0.93–1.28)	0.95 (0.70–1.29)	1.06 (0.82–1.35)
Other	1.03 (0.97–1.10)	1.08 (0.99–1.14)	1.00 (0.93–1.07)
RR (95% CI) of mortality on lag day 3 with increased SO_2[b]			
Total	1.04 (0.99–1.08)	1.01 (0.96–1.07)	1.03 (0.99–1.08)
Respiratory	1.00 (0.91–1.10)	0.97 (0.87–1.09)	1.01 (0.92–1.12)
Cardiovascular	1.20 (1.11–1.30)**	1.18 (1.07–1.30)**	1.20 (1.10–1.30)**
Cancer	0.94 (0.74–1.18)	1.02 (0.76–1.37)	0.90 (0.70–1.17)
Other	0.99 (0.85–1.06)	0.96 (0.88–1.04)	0.97 (0.90–1.04)

[a]Excluding mortality values on 3 extreme days plus pollution measurements on the same day and all 5 days previous to each. [b]Relative risk (RR) associated with a 100 μg/m^3 increase in daily mean SO_2 concentration estimated using robust Poisson regression with allowance for overdispersion and adjustment for trend, season, weather, and day of the week. *$p < 0.02$, **$p < 0.002$.

the gases (and particularly CO, but not O_3) were much more strongly associated with mortality than was PM (Moolgavkar 2000). Goldberg et al. (2001) found that the 3-day mean of O_3 was associated with total nonaccidental mortality as well as deaths specifically from neoplasms, lung cancer, cardiovascular diseases, coronary artery disease, and respiratory diseases after adjusting for concentrations of CO_2, CO, NO_2, SO_2, and coefficient of haze. Burnett at al. (1998b) observed statistically significant positive associations between daily mortality in Toronto, Canada, and ambient levels of CO, NO_2, SO_2, coefficient of haze, TSP, sulfates, and estimated $PM_{2.5}$ and PM_{10} over the 15-year period from 1980 to 1994. However, in multipollutant models, the effects of air pollution on excess deaths could almost completely be explained by the levels of CO and TSP.

These results have led some authors to conclude that the pollutants measured and included in models of daily mortality might better be interpreted as indicators of the biologically relevant pollutant mixture and that the best indicators might differ between geographic areas. Moolgavkar (2000) reported that in Los Angeles County over the period 1987–1995, the association of SO_2 with daily mortality was very strong and robust to control of particulates (either PM_{10} or $PM_{2.5}$). However, the estimated effect of SO_2 on mortality was unusually large (a 3.6% increase in daily mortality associated with a 3 ppb increase in ambient SO_2 concentrations). Given that such an extreme effect of SO_2 on daily mortality seemed unlikely, he concluded that SO_2 is most likely an indicator of a pollution source or, more generally, of the mixture of pollutants that is associated with daily mortality. In a large and comprehensive meta-analysis, Stieb et al. (2002) found that the effect sizes estimated in multipollutant models were generally less than those from single-pollutant models. They suggested that because of covariation between pollutants, the lower bound results from multipollutant estimates cannot simply be interpreted as the independent effect of a given pollutant and suggested that assessing the overall effect of the air pollution mix may be both more meaningful and more achievable than attempting to isolate the effect of individual pollutants.

A limitation of our study is that we did not measure other pollutants, including CO, O_3, and NO_2. Although SO_2 might be directly increasing the risk of mortality in our population, our results might also indicate that SO_2 concentrations are correlated with the relevant pollutant mixture concentrations (that might or might not include SO_2) in Chongqing.

We found positive and statistically significant associations between daily ambient SO_2 and cardiovascular or respiratory mortality, but associations with deaths due to cancer or other causes were statistically insignificant and not consistently positive. Although previous studies have consistently reported pollution effects specific to respiratory mortality, reports of greater effects on cardiovascular mortality have been less consistent. A recent meta-analysis by Stieb et al. (2002) reported that the pooled effect size for respiratory mortality was larger than that for total nonaccidental mortality for all pollutants (CO, SO_2, nitrogen monoxide, and PM) other than O_3. However, the pooled effect sizes for any pollutants were not significantly larger for cardiovascular mortality than were the corresponding effect sizes for total nonaccidental mortality. Although the biologic pathways through which air pollution might increase the risk of cardiovascular mortality require further study, some cardiorespiratory pathophysiologic effects of air pollution that could increase the risk of cardiovascular disease and mortality have been observed in humans (Stieb et al. 2002). Measures of ambient air pollution have been associated with poor cardiac autonomic control in the elderly (Liao et al. 1999), increased heart rate (Peters et al. 1999a), increased systolic blood pressure (Peters et al. 1999b), increased plasma fibrinogen (Pekkanen et al. 2000), increased plasma viscosity (Peters et al. 1997), and possible sequestration of red cells in the circulation (Seaton et al. 1999). Our results are consistent with the expectation that persons with serious respiratory or cardiovascular diseases should be those who are most sensitive to the biologic effects of air pollution.

We recognize a limitation of our study: We had daily SO_2 measurements for the entire year but $PM_{2.5}$ measurements for only 7 months. Therefore, our models had more power to detect an association of mortality with SO_2 than with $PM_{2.5}$. Also, when we tested the effect of controlling for $PM_{2.5}$ on our positive and significant SO_2 results, we set missing values of $PM_{2.5}$ to zero and added a dummy variable to represent days without $PM_{2.5}$ observations in addition to a term for $PM_{2.5}$ concentration. We were therefore controlling $PM_{2.5}$ with less information than we had for SO_2. However, when we limited our analysis only to days with both SO_2 and $PM_{2.5}$ observations, the positive associations between SO_2 and mortality were slightly strengthened by controlling for $PM_{2.5}$ in our models (data not shown).

When we reanalyzed our data after excluding 3 days with extremely high mortality counts and pollution concentrations on each of these days and the 5 days before each, the associations between SO_2 and mortality due to cardiovascular and respiratory causes on the second lag day were no longer statistically significant (Table 5). Figure 2 shows that high mortality counts on observation days 52 and 60 were both preceded 2 days earlier by peak concentrations in mean SO_2. In contrast to the change in the significance of effect estimates on the second lag day, those on the third lag day were unaffected by the exclusion of high-mortality days (Table 5). These results suggest the possibility that on peak pollution days, the effect of SO_2 (or the pollution mix for which it is acting as an indicator) on cardiovascular and respiratory mortality risk was relatively greater than on days with lower concentrations. However, because our data included so few peak mortality days, we cannot confidently make this conclusion.

We recognize a limitation inherent to all ecologic time-series analyses of multiple, correlated air pollutants: Ambient concentrations

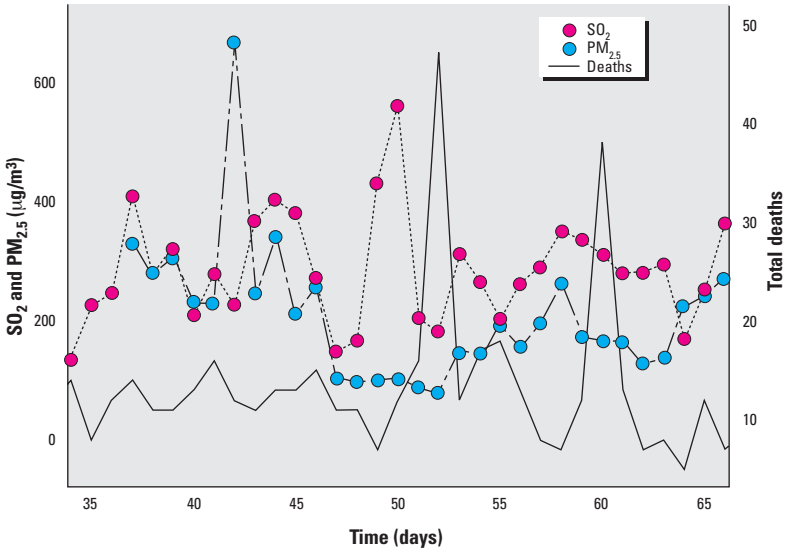

Figure 2. Daily SO_2, $PM_{2.5}$, and total mortality from 3 February to 7 March 1995.

of $PM_{2.5}$ and SO_2 measured at centrally located sites were used to estimate the average population exposure to these pollutants. Although we believe it is reasonable to consider these measurements as good proxies for the true, biologically relevant population exposures, the differences between these proxy values and the true exposures are an inherent and unavoidable type of measurement error. This error can bias effect estimates in ecologic time-series analyses and have been described previously (Zeger et al. 2000). In most circumstances, if pollutants have true causal effects, then their effect estimates will be biased toward zero in the presence of this type of measurement error. However, when multiple pollutants are modeled simultaneously, it is possible that some of the effect estimate of a pollutant with a true effect can be transferred to the effect estimate of a pollutant with no true effect, causing a bias away from zero. This transfer generally can occur from a pollutant measured with more error to one measured with less. However, in order for this transfer to be large, the true population exposures to the two pollutants or the measurement errors in each pollutant need to be highly correlated. In our study, measured $PM_{2.5}$ and SO_2 had a correlation coefficient of 0.45 on the days with observations of both pollutants. However, because we were unable to measure true population exposures, we were not able to determine either the correlation of true $PM_{2.5}$ and SO_2 exposures or the correlation of measurement errors in each pollutant. Despite this limitation, the large estimated effects of SO_2 in contrast to the statistically insignificant and sometimes negative estimated effects of $PM_{2.5}$ suggest that the observed associations between daily mortality risk and SO_2 were unlikely to have been due to bias away from zero caused by correlation of true exposures to $PM_{2.5}$ and SO_2 or their measurement errors.

We conclude that, in this population, daily ambient SO_2 concentrations were positively and significantly associated with population risks of cardiovascular and respiratory mortality, even after controlling for daily ambient $PM_{2.5}$. Regardless of whether SO_2 directly increases the risk of mortality in this population or is a correlated indicator of the biologically relevant air pollution mixture (that might or might not include SO_2), our results support the conclusion that consistent associations between SO_2 and daily mortality found in previous Chinese studies appear not to have been confounded by unmeasured fine particles.

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