Mortality and Ambient Fine Particles in Southwest Mexico City, 1993–1995

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Epidemiologic studies have focused attention on the health effects of fine particulate air pollutants <2.5 μm in diameter ($PM_{2.5}$). To further characterize the potential effects of fine particles, we investigated the relationship of air pollution to mortality in Mexico City during 1993–1995. The concentration of $PM_{2.5}$ was measured on a 24-hr integrated basis; concentrations of NO_2 and ozone were measured hourly and reduced to 24-hr means. Daily mortality was determined from death registration records, and Poisson regression was used to model daily death counts as a function of air pollutant levels on the same and previous days, while controlling for temperature and periodic cycles. Without taking other air pollutants into account, a 10 μg/m^3 increase in the level of $PM_{2.5}$ was associated with a 1.4% increase in total mortality, both on the current day and 4 days after exposure [95% confidence interval (CI), 0.2–2.5]. An equivalent increase in $PM_{2.5}$ was also associated with somewhat larger excesses of deaths among people over 65 years of age and from cardiovascular and respiratory causes, which occurred after a lag of 4 days. The mean concentration of ozone over a 2-day period was associated with a 1.8% increase in mortality from cardiovascular diseases. NO_2 was not consistently related to mortality. Fine particles had an independent effect on mortality when modeled simultaneously with other pollutants, and the association of ozone with cardiovascular mortality was strengthened after adjusting for NO_2 and $PM_{2.5}$. These results support previous findings that urban air pollution at current levels leads to excess mortality and suggest that fine particles may play a causal role in producing that excess.
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Epidemiologic time–series studies indicate that increased mortality is associated worldwide with high levels of particulate air pollution on the same day or the days immediately before. A review of 20 such studies for the EPA criteria document on particulate matter (*1*) indicated that, on average, all-cause mortality increases 2.5–5% for each increment of 50 μg/m^3 in the ambient concentration of thoracic particles (particulate matter <10 μm in aerodynamic diameter, or PM_{10}). Epidemiologic findings have been remarkably consistent across studies, and similar estimates have been reported in independent meta-analyses by several authors (*2–5*). These observed increases in total mortality appear to be due in part to more strongly elevated risk among the elderly and for cardiovascular and respiratory disease mortality (*2,6*).

A key development in recent studies is the observation that the overall effects of thoracic particles may be largely attributable to the fine fraction less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$). Two large, prospective studies (*7,8*) found associations between fine particles and mortality in selected cities in the United States. In a subsequent analysis, mortality increased 7.5% for each 50 μg/m^3 of fine particles and was stronger than the effect of total thoracic particles or sulfates (*9*). Nevertheless, the number of studies that have examined the link between fine particles and mortality is small, and all of them have been conducted in the United States, in cities with a relatively limited range of climatic and population characteristics.

To further examine the evidence that fine particulate air pollution is associated with excess mortality, we conducted an epidemiologic time–series study in the southwestern part of Mexico City, where we made daily air pollution measurements during the years 1993–1995. Mexico City is one of the world's most populous urban areas, with 18 million inhabitants, some 3 million motor vehicles, and over 4,000 industrial establishments sharing the metropolitan zone of the Valley of Mexico (*10*). Owing to its location at 19°N latitude and 2,200 m above sea level, Mexico City has a mild tropical climate with temperatures very rarely outside the range of 0–35°C. Since buildings are generally not heated, air pollution is primarily from automotive and industrial sources (*10*). Relative to other urban areas in North America and Europe, Mexico City has low levels of sulfur dioxide, levels of particles that can be moderately to very high, but vary by area of the city, and very high levels of ozone. In addition, the population is younger, with a lower crude death rate and a different epidemiological profile. Research in this setting can be particularly informative because of its differences from the sites of previous studies.

In a previous study in Mexico City, we observed a relative risk for total mortality of 1.06 per 100 μg/m^3 total suspended particles, with no independent effect of ozone despite its high levels (*11*). However, the ability to characterize the effect of particles was limited by the lack of information about finer size fractions and by the air monitoring scheme in use at that time, which provided particulate data only every sixth day. With daily measurements of the possibly more potent fine particles available for the current study, our hypothesis was that increasing levels of fine particles are associated with excess mortality, independent of ozone.

Methods

Study area. The research area was formed from six geopolitical subunits of the Federal District of Mexico (Delegaciones Alvaro Obregón, Benito Juárez, Coyoacan, Cuajimalpa, Magdalena Contreras, and Tlalpan) surrounding an air quality monitoring station that we operated at a school in the southwestern part of the city (*12*). This area has about 2.5 million inhabitants (about one-third the population of the Federal District) and is socioeconomically diverse, including both poor neighborhoods and some of the city's wealthiest areas. Historically, the southwest has tended to have the highest ozone concentrations in the city and lower levels of particulates than heavily industrialized areas in the northwest (*10*).

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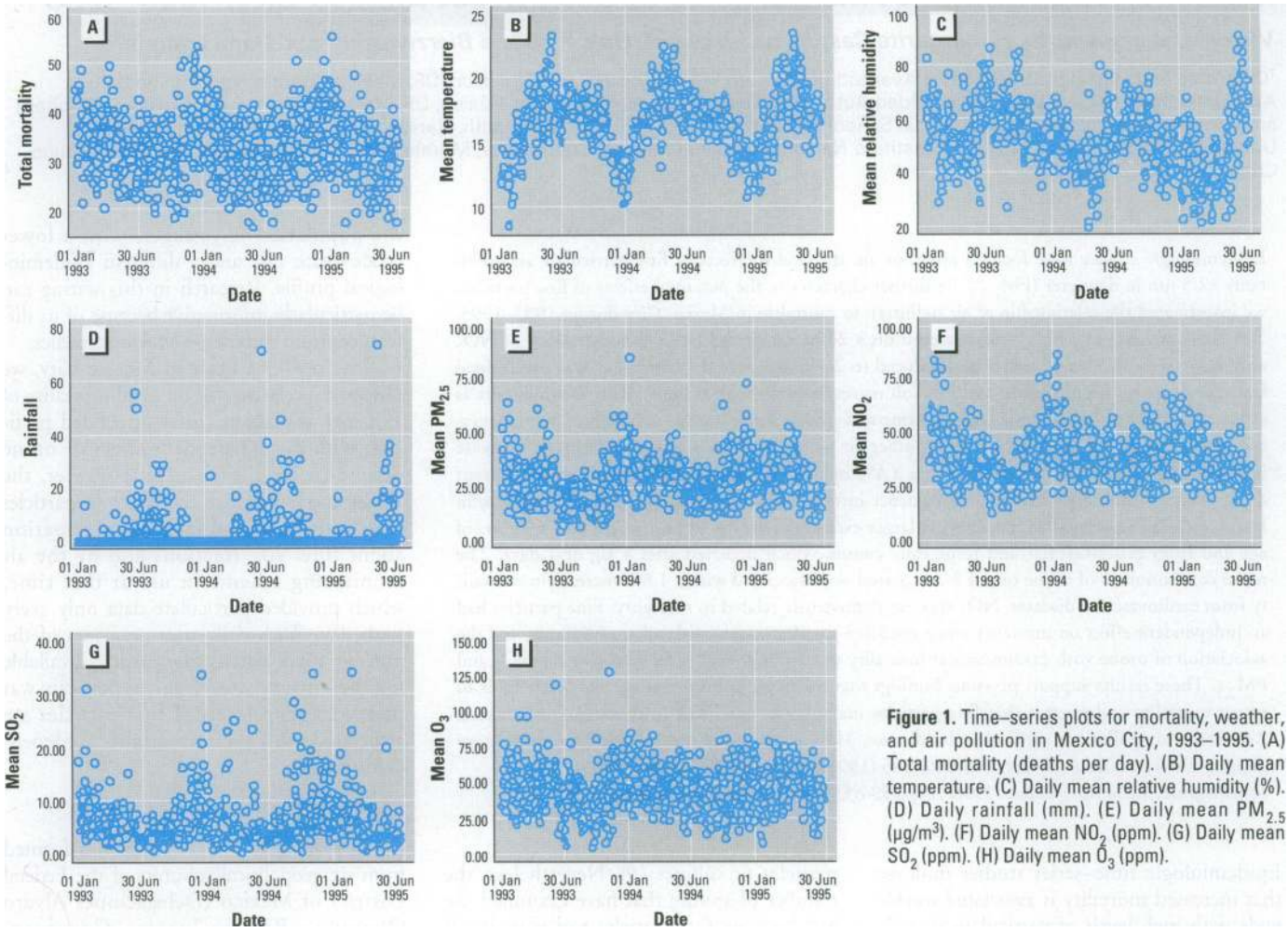

Figure 1. Time–series plots for mortality, weather, and air pollution in Mexico City, 1993–1995. (A) Total mortality (deaths per day). (B) Daily mean temperature. (C) Daily mean relative humidity (%). (D) Daily rainfall (mm). (E) Daily mean $PM_{2.5}$ ($\mu g/m^3$). (F) Daily mean NO_2 (ppm). (G) Daily mean SO_2 (ppm). (H) Daily mean O_3 (ppm).

Mortality data. Electronic records of death certificates of residents of the six delegaciones of the study were obtained from the Instituto Nacional de Estadística, Geografía, e Informática. The record for each decedent included age, place of residence, and the date, place, and underlying cause of death. Causes of death were coded according to the 9th revision of the *International Classification of Diseases* (ICD-9). Deaths from external causes (accidents, poisoning, and violence), indicated by ICD-9 codes >E800 were excluded, as were those which occurred outside the Federal District.

The death data were reduced to daily counts of deaths for all ages and for all nonexternal causes of death combined. Daily deaths were reaggregated to obtain the numbers of deaths for persons ≥65 years of age and for the cause categories of respiratory disease (ICD-9 codes 460–466, 480–487, 490–496, 500–508), cardiovascular disease (ICD-9 codes 390–398, 401–417, 420, 430–438, 440–448), and all other causes.

Air quality data. Ambient air pollutant levels were monitored at a station we operated at a primary school in Pedregal, a residential area in the southwest. Levels of fine particles ($PM_{2.5}$) were recorded as 24-hr integrated particle mass, with samples collected on Teflon filters using Harvard Impactor low flow size-fractionated particle samplers. Filters were collected daily at 0800 hr, and particle mass was determined gravimetrically in a temperature- and humidity-controlled laboratory according to a standard protocol. Field and laboratory filters were used to detect problems in sampling and mass determination. A 10% co-located sample was used to ensure sampling precision.

Concentrations of O_3, NO_2, NO_x, NO, and SO_2 were measured hourly using U.S. EPA standard methods: ultraviolet photometry for ozone, chemiluminescence for nitrogen oxides, and pulsed fluorescence for SO_2. Instruments were calibrated bimonthly.

External audits of all monitoring systems were performed twice a year by the Harvard School of Public Health, Cambridge, Massachusetts. Pollutant measurements that failed to meet quality assurance criteria were excluded from the epidemiologic study.

Meteorological data were provided by José Camacho Salazar (personal communication) from a station operated by the Observatorio Meteorológico del Colegio de Geografía of the Universidad Nacional Autónoma de México. Temperature and relative humidity were measured hourly by automatic recording instruments, and rainfall was measured daily with a conventional rain gauge. All methods were standard, and co-located reference instruments were used for calibration.

Hourly measurements of air pollution and weather parameters were reduced to 24-hour means, with daily minimum and maximum temperature also retained as additional indicators.

Data analysis. Except for occasional missing or excluded observations, data for all air pollutants were available for the period 1 January 1993–31 July 1995. The mortality and air quality data were merged to create an analysis file with days as the units of observation. We used the 24-hr mean as the indicator of exposure to all air pollutants. Although prevailing standards for ozone are based on the daily 1-hr maximum concentration, the daily mean was a better predictor of mortality in our previous study in Mexico City (*11*), in addition to being more

consistent with the indicators for other pollutants. The distributions of mortality, air pollution, and weather parameters were initially examined one at a time using descriptive statistics and one-way plots; the temporal behavior of each variable was described with time–series plots.

Mortality is a rare event whose frequency varies as a continuous function of time-related factors such as weather. We therefore used an extension of Poisson regression to model daily mortality. To allow for nonlinear relationships between mortality and predictor variables related to time and climate, we employed a generalized additive model, which allows the linear predictor, X, in the conventional Poisson regression model, $\log[E(Y)] = \beta X$, to be replaced by a smooth, nonlinear function of the predictor variables or a combination of linear and nonlinear predictors (*13*). Because the form of the function governing the behavior of mortality over time is unknown, we developed nonparametrically smoothed functions of predictor variables empirically using standard smoothing algorithms. Other investigators have used similar models (*14,15*). For the models used in the analyses presented here, we used the LOESS smoother (*16*), but comparable results were achieved using other smoothing methods.

Mortality on successive days may be correlated because of the dependence of death rates on weather and other cyclical factors. To account for the potential effects of these serial correlations among observations, we multiplied the estimated variance of the regression coefficients by the square root of the overdispersion parameter (*17*) to adjust for extra-Poisson variation (*16*). Stata software (Stata Corporation, College Station, TX) was used for data management and convential Poisson regression, and S-Plus (Statistical Sciences Corporation, Seattle, WA) was used to fit generalized additive models.

As the first step in the model-building process, we developed a basic predictive model for daily mortality, without regard to air pollution. We examined relationships of time, temperature, humidity, and rainfall to mortality using a combination of graphical and regression methods. We considered smoothed functions of minimum, maximum, and mean temperature on the current day and lagged up to 6 days, 3-day moving averages of temperature with lags of 0–2 days, and an array of variables for humidity and rainfall.

In comparing regression models, we evaluated both goodness of fit and the magnitude of regression coefficients, giving the greatest weight to parameters with large coefficients in models that fit the data well. Goodness of fit was evaluated by Akaike's Information Criterion (AIC), a measure of model deviance (a conventional indicator of fit) (*17*) adjusted for the number of parameters (*13*).

Pollution variables were added after developing the basic mortality model. Fine particles were of primary interest, but we also considered NO_2 and O_3 as independent predictors and potential confounders. SO_2 was not considered because the concentrations were comparable to those in the cities with the lowest levels, as reported in other studies (*4,7,18–20*). Pollutant concentrations were entered as continuous variables scaled in micrograms per cubic meter for particles and parts per billion (ppb) for gases. To examine the temporal relation between pollution and mortality, we considered mean exposures in moving "windows" (*21*) of 1–5 days duration. For each pollutant, the window associated most strongly with each category of mortality was used in the final model.

Regression coefficients describing the relationship of mortality to pollutant levels were expressed as the percent change in mortality per 10 unit (micrograms per cubic meter or ppb) change in concentration for all pollutants. These increments were equivalent to 0.7 interquartile range (IQR) for fine particles, 2.4 IQR for SO_2, 0.7 IQR for NO_2, and 0.5 IQR for O_3. Ninety-five percent confidence intervals (CIs) for the coefficients were estimated using the normal approximation.

Results

Descriptive analysis. On the average day, there were 32 deaths in the study area, including 18 among people ≥65 years of age, 3 from respiratory causes, and 9 from cardiovascular diseases (Table 1). Daily mean temperature and relative humidity had rather narrow ranges, with means of 16.5°C and 51.6%, respectively (Table 2). The mean concentration of fine particles was 27 $\mu g/m^3$. Concentrations of NO_2 and SO_2 were moderate to low, with means of 37.7 and 5.6 ppm, respectively. In contrast, the level of O_3 was high: the mean was 44.0 ppm and the 1-hr maximum concentration exceeded prevailing standards on the majority of days (Table 2).

Current day levels of most pollutants were moderately to strongly correlated, with Pearson correlation coefficients ranging from 0.52 to 0.71 (Table 3). The correlation of ozone with other pollutants was diminished when lagged pollutant levels were used, while correlations between the remaining pollutants were essentially unchanged (Table 3). Regardless of the lag period, the strongest correlations were between fine particles and NO_2 (Table 3).

Mortality displayed a marked seasonal pattern peaking in January (Fig. 1A). Temperature, relative humidity, and rainfall had an opposite pattern, with minimums early in the year and peaks in June or July (Fig. 1B-D). The seasonality of rainfall was particularly pronounced, with the majority occurring between June and October (Fig. 1D). Like mortality, particulate pollutant levels peaked early in the year, then declined during the rainy season (Fig. 1E). Seasonal patterns were similar for NO_2 and SO_2 (Fig. 1F-G), but notably less distinct for ozone (Fig. 1H).

Mortality model. Of the array of weather variables that we considered in the initial phase of model building, smoothed functions of minimum temperature lagged 2 days, mean temperature lagged 1 day, and the average temperature during the 3 days before death were the strongest predictors of mortality, indicating a linear 0.20–0.27% decrease in mortality per degree Celsius. Relative humidity and rainfall were also associated with mortality when considered in conventional multivariable Poisson regression models. However, three-dimensional plots suggested that these variables were strongly related to temperature. When all three variables were assessed simultaneously, temperature was associated most strongly with mortality, and its effect was the same regardless of whether humidity or rainfall was in the model. Smoothed three-dimensional surfaces combining temperature and humidity gave analogous results. We also evaluated short-term time effects by adding indicator variables for day of the week to the Poisson regression model, but they had no appreciable effect.

The best compromise between model fit and number of parameters was achieved with a model containing nonparametrically smoothed terms for time and the mean temperature during the 3 days before death. A similar model with only the time term fit nearly as well, but the quality of fit diminished in models containing only variables for temperature on the same day, or up to 3 days previously. Adding relative humidity to the model with smoothed time and temperature did little to improve fit, and the fit actually deteriorated when an indicator variable for season was added. As a result, we adopted the model containing smoothed terms for time and the mean temperature during the 3 days before death as the basic model for futher analyses.

Fine particles. A 10 $\mu g/m^3$ increase in fine particles was associated with 1.3% increase in total mortality on the same day (CI, 0.2–2.5) and a 1.4% increase after a lag of 4 days (CI, 0.2–2.5), but no excess mortality was associated with fine particles

on intervening days (Table 4). When multiple-day exposure windows were examined, total mortality was associated most strongly with the mean exposure of the previous 5 days (1.5% change per 10 $\mu g/m^3$). However, precision was reduced relative to single-day windows (Table 4), so we used the daily mean concentration 4 days previously as the index of exposure to fine particles in subsequent analyses.

Fine particles 4 days previously were associated with a 1.6% increase in deaths among people over 65 years of age (CI, 0.0–3.1). Similar patterns were observed for respiratory mortality, with a 2.5% increase in deaths associated only with fine particles 4 days previously, and also for cardiovascular diseases, with a 2.2% increase in deaths associated with fine particles 4 days earlier (Table 5).

Other air pollutants. A 10 ppb increment in the level of ozone was associated with <1% change in total mortality for all exposure windows (data not shown). Of the windows examined, the mean concentration of ozone in the 1–2 day period was the best predictor of mortality. With this indicator, cardiovascular disease deaths increased 1.8% per 10 ppb (CI, 0.1–3.5), while the changes for other categories of mortality were <1% (Table 5).

For NO_2, the mean concentration during the previous 1–5 days was associated most strongly with mortality. A 10 $\mu g/m^3$ change in NO_2 during this period was associated with roughly 1% changes in total mortality and cardiovascular mortality and a 2% change in respiratory mortality (Table 5). The precision of these estimates was relatively poor, however (Table 5).

Multiple air pollutants. To evaluate the evidence for independent effects of the three pollutants, we fit models simultaneously containing variables for fine particles, O_3 and NO_2 in combinations of two and three. The two-pollutant model including fine particles and ozone yielded essentially the same results as one-pollutant models for the same constituents, with 1–2% increases in total, elderly, respiratory, and cardiovascular mortality for a 10-unit increase in particles, and a 2% increase in cardiovascular mortality for ozone (Table 5). The results for particles were also similar in a two-pollutant model that also included NO_2, with little evidence that NO_2 was associated with any cause of death. With variables for all three pollutants in the model simultaneously, the results were again similar to those obtained when pollutants were considered one or two at a time. A 10-unit increment in fine particles was associated with a 1.7% increase in total mortality (CI, 0.2–3.1%), a 2.3% increase in mortality among the elderly (CI, 0.3–4.2), and a 3.4% increase in cardiovascular disease mortality. The association of ozone with cardiovascular mortality was strengthened and became statistically significant; a 10-unit change in ozone was associated with a 2.8% change in cardiovascular mortality (CI, 0.0–5.6%). This model again gave little evidence of an association of mortality with NO_2.

Discussion

We found that a 10 $\mu g/m^3$ increase in the concentration of fine particles was associated with a 1.3–1.7% increase in total mortality 4 days after exposure, regardless of the presence of other air pollutants. The same level of increase in fine particles was also associated with excess mortality of around 2% among people over 65 years of age and from cardiovascular and respiratory causes, all occurring after a lag of 4 days. Rising levels of ozone were associated with rising mortality from cardiovascular diseases, which increased about 3% per 10 ppb of ozone. Ozone was not associated with other causes of death, however.

The association of fine particles and mortality was bimodal in time, with an acute increase in mortality on high pollution days, followed by a second peak 4 days later. This phenomenon is consistent with both a "harvesting" of highly susceptible persons on the day of exposure to high pollution levels and a lagged increase in mortality due to delayed effects of reduction of pulmonary defenses, cardiovascular complications, or other homeostatic changes among less-compromised individuals.

These findings are based on a statistical model for mortality that controlled periodic variations in death rates with a small number

Table 1. Summary statistics for daily mortality by age and cause of death in southwest Mexico City, 1993–1995

	Total	Age ≥65 years	Cardiovascular diseases	Respiratory diseases	Other causes
Mean	32	17.8	9.1	3.2	19.8
Standard deviation	6.4	4.7	3.2	1.9	4.7
Minimum	16	4	1	0	6
Lower quartile	27	15	7	2	16
Median	32	17	9	3	20
Upper quartile	51	21	11	4	23
Maximum	55	36	20	11	39

Table 3. Pearson pairwise correlation coefficients among air pollutants on the same day and on the day associated most strongly with mortality for each pollutant

	$PM_{2.5}$	NO_2
Same day		
NO_2	0.71	
O_3	0.59	0.46
Mortality-associated day	$PM_{2.5}$, 4-day lag	NO_2, 5-day mean
NO_2, 5-day mean	0.57	
O_3, 2-day mean	0.22	0.39

Table 2. Summary statistics for mortality, air pollutant concentrations, and weather indicators, southwest Mexico City, 1993–1995

	$PM_{2.5}$ ($\mu g/m^3$)	O_3 (ppb)	O_3, 1 hr maximum (ppb)	SO_2 (ppb)	NO_2 (ppb)	Minimum temperature (C)	Mean temperature (C)	Relative humidity (%)	rainfall (mm)
Valid observations	866	901	926	877	861	942	942	932	942
Mean	27	44.04	163	5.58	37.70	9.1	16.5	51.6	2.3
Standard deviation	11	15.66	57	4.52	11.35	3.3	2.4	12.3	6.5
Minimum	4	4.09	12	0.00	12.83	-1.2	8.3	19.0	0.0
Lower quartile	20	33.67	125	2.79	29.12	6.7	15.0	42.8	0.0
Median	26	43.71	164	4.17	36.29	9.5	16.7	51.9	0.0
Upper quartile	34	54.21	202	7.00	43.96	12.0	18.0	59.8	1.2
Maximum	85	127.07	342	33.92	86.83	17.2	23.3	91.0	73.3
U.S. standard[a]	65	–[b]	120	140	53	–	–	–	–

Deaths, pollutant levels, and meterological paramaters expressed as 24-hr means except as noted; observed pollutant levels given under local conditions.
[a]1997 U.S. National Ambient Air Quality Standard, based on 24-hr average for $PM_{2.5}$ and SO_2, maximum 1-hr concentration for O_3, and annual average for NO_2.
[b]Indicates no standard for the parameter.

of parameters based on known relationships between weather and mortality. Poisson regression models fit the data well, with overdispersion parameters typically in the range of 1.10–1.12. As in a previous study in Mexico City (*11,22*), temperature was the strongest weather-related predictor of mortality, and the death rate increased with low temperatures, but not with high ones. Daily mean temperatures in Mexico City fall into a relatively narrow range, with the highest mean daily temperatures observed during the study period substantially lower than those seen in such cities as Philadelphia, Pennsylvania, and Los Angeles, California (*15,23*). Consequently, we did not observe the ascending limb of the well-known "j"-shaped curve that describes the relationship of temperature and mortality in temperate areas (*24*).

It is also noteworthy that despite Mexico City's reputation for polluted air, in the study area only the level of ozone was remarkably high by current standards. The mean concentration of fine particles in the study area was similar to that reported in Steubenville, Ohio (*7*). While comparable to those of the dirtier cities in recent studies in the United States (*7,8*), the study area's particle concentrations were substantially lower than the levels observed in contemporary studies of Santiago, Chile, and São Paulo, Brazil (*25,26*), and far lower than those that existed historically in industrial cities like London (*4*).

These findings from Mexico City provide further evidence that fine particles are associated with total mortality and with mortality among the elderly. In addition, they are consistent with our expectation, based on a previous study with less complete information on exposure to total suspended particles (*11*), that increases in total mortality would be associated with increasing particulate pollution, but not with increasing ozone. Despite the substantial differences in environmental, population, and epidemiological characteristics between Mexico City and other areas where the health effects of fine particles have been studied, our results for total mortality are virtually identical to the 1.5% per 10 $\mu g/m^3$ increase in fine particles reported in analyses of data from the Six Cities Study in the United States (*9*). Our study differs from previous research of the relationship of fine particles and mortality in the United States (*7–9*), however, in that we employed a time–series approach rather than a standard cohort design.

While it is plausible that ambient ozone might affect mortality, research on this topic has been limited in comparison to the abundant information available on the effects of particulate matter on mortality. Recent studies from the United States (*15,27*), Europe (*28–31*), and Australia (*32*) have found positive associations with same-day ozone and ozone lagged 2 days, with relative risks from 1.05 to 1.07 per 100 $\mu g/m^3$. Most of these reports evaluated the effect of ozone controlling for other

Table 4. Percent increase in daily total mortality, 95% confidence interval (CI), and *t*-statistic associated with a 10 $\mu g/m^3$ increment in fine particles ($PM_{2.5}$) or a 10 ppb increment in ozone, estimated by Poisson regression controlling for temperature on the 3 days before death and smoothed periodic cycles

Pollutant	Percent increase	CI	*t*-Statistic[a]
$PM_{2.5}$			
Same-day exposure	1.34	0.16–2.52	2.23
Exposure lagged 1 day	-0.16	-1.33–1.02	-0.26
Exposure lagged 2 days	0.41	-0.74–1.56	0.70
Exposure lagged 3 days	0.43	-0.74–1.60	0.72
Exposure lagged 4 days	1.36	0.20–2.52	2.30
Exposure lagged 5 days	0.99	-0.19–2.18	1.65
Mean exposure during previous 5 days	1.48	-0.01–2.96	1.95
O_3			
Same-day exposure	0.37	-0.39–1.13	0.95
Exposure lagged 1 day	0.22	-0.55–0.98	0.55
Exposure lagged 2 days	0.48	-0.28–1.24	1.23
Exposure lagged 3 days	0.04	-0.74–0.81	0.09
Exposure lagged 4 days	0.19	-0.58–0.96	0.49
Exposure lagged 5 days	0.24	-0.54–1.01	0.60
Mean exposure during previous 2 days	0.63	-0.27–1.53	1.37

All statistics adjusted for overdispersion.
[a]With 1 degree of freedom.

Table 5. Percent increase in daily mortality for exposure to $PM_{2.5}$, NO_2, and O_3

	One pollutant models			Two pollutant models						Three pollutant model		
				$PM_{2.5} + O_3$			$PM_{2.5} + NO_2$					
Outcome	Percent change	CI	*t*	Percent change	CI	*t*	Percent change	CI	*t*	Percent change	CI	*t*
$PM_{2.5}$ (4-day lag)												
All causes, all ages	1.36	(0.20–2.52)	2.30	1.44	(0.25–2.63)	2.37	1.33	(-0.12–2.78)	1.80	1.68	(0.23–3.14)	2.27
Age >65 years	1.58	(0.04–3.12)	2.01	1.61	(0.01–3.20)	1.98	1.81	(-0.11–3.74)	1.85	2.27	(0.32–4.21)	2.28
Respiratory causes	2.50	(-1.12–6.11)	1.35	2.64	(-1.08–6.35)	1.39	2.00	(-2.48–6.47)	0.88	1.68	(-2.88–6.24)	0.72
Cardiovascular causes	2.19	(-0.01–4.38)	1.95	2.22	(-0.04–4.48)	1.92	1.68	(-2.88–6.24)	0.72	3.42	(0.67–6.18)	2.43
Other noninjury causes	0.78	(-0.70–2.26)	1.04	0.85	(-0.66–2.37)	1.10	0.70	(-1.15–2.54)	0.74	0.86	(-1.00–2.71)	0.90
O_3 (mean 1–2 days previously)												
All causes, all ages	0.63	(-0.27–1.53)	1.37	0.57	(-0.62–1.76)	0.94				0.73	(-0.73–2.18)	0.98
Age >65 years	0.82	(-0.39–2.03)	1.32	0.70	(-0.89–2.29)	0.86				1.10	(-0.85–3.05)	1.11
Respiratory causes	-0.74	(-3.58–2.10)	-0.51	-1.05	(-4.77–2.66)	-0.56				-1.61	(-6.17–2.94)	-0.69
Cardiovascular causes	1.76	(0.07–3.46)	2.04	2.07	(-0.19–4.33)	1.79				2.79	(0.04–5.55)	1.99
Other noninjury causes	0.30	(-0.85–1.44)	0.50	0.13	(-1.39–1.64)	0.16				0.14	(-1.72–2.00)	15
NO_2 (mean 1–5 days previously)												
All causes, all ages	1.14	(-0.49–2.76)	1.37				0.01	(-2.09–2.12)	0.01	-0.07	(-2.67–2.53)	-0.05
Age >65 years	0.75	(-1.44–2.93)	0.67				-0.65	(-3.45–2.16)	-0.45	-1.11	(-4.61–2.39)	-0.62
Respiratory causes	2.32	(-2.71–7.35)	0.91				1.17	(-5.34–7.69)	0.35	0.29	(-0.29–0.87)	0.97
Cardiovascular causes	1.41	(-1.65–4.47)	0.90				-0.68	(-4.68–3.31)	-0.34	-0.45	(-5.34–4.45)	-0.18
Other noninjury causes	0.75	(-1.32–2.81)	0.71				0.11	(-2.57–2.78)	0.08	-0.01	(-3.32–3.30)	-0.01

Estimated by Poisson regression controlling for temperature on the 3 days before death and smoothed periodic cycles.
CI, 95% confidence interval; *t*, *t*-statistic with 1 degree of freedom. All statistics adjusted for overdispersion.

pollutants such as black smoke or PM_{10} (*15,28–31*), but none of them assessed the effect of ozone independent of fine particles. Contrasting results were reported by Kinney and Ozkaynak (*20*), who noted an initial, positive association of total mortality with ozone levels in long-term studies of ozone and mortality in Los Angeles and New York, which was eliminated when a term for particles was added to regression models in subsequent analyses of the data from Los Angeles (*23*).

Our finding in this study that ozone was a significant predictor for cardiovascular mortality but not for mortality due to respiratory causes is similar to the meta-analysis of the APHEA project (*28*), but contrasts with other studies that have examined specific causes of death (*31*). Kelsall et al. (*15*) reported statistically independent associations between ozone and total daily mortality in an analysis of data from Philadelphia, but associations with cardiovascular and respiratory causes did not achieve statistical significance.

Differences in climate and the composition of the air pollution mixture may underlie the distinct epidemiological findings for ozone in Mexico City. Ozone concentrations do not show strong seasonal patterns in Mexico City; levels are high all year, which may lead to chronic exposure at higher levels than elsewhere. Additionally, we found a positive correlation of ozone and fine particles, rather than the negative correlations typically seen in Europe and the United States. The possibility of errors in classifying causes of death should also be considered in interpreting our results for cause-specific mortality. The data we used gave only the underlying cause of death, which may not reflect acute mechanisms of death among people with chronic conditions such as cancer. The underlying cause of death may also be miscoded in some cases. A detailed study of Mexico City death certificates for the years 1991 and 1994 suggested that 12% of deaths might be misclassified among broad categories such as respiratory and cardiovascular causes (*22*).

Due to the design of this study, we could not draw any conclusions about whether individuals dying on high pollution days had high personal exposure to pollutants or identify mechanisms by which air pollution might cause death. We had no information about individual exposure or medical status. In addition, we studied only short-term relationships between mortality and pollution on a daily basis and could not observe the long-term effects of exposure to air pollution. Nevertheless, the study's aggregate time–series design conferred several advantages. The need to control for external predictors of mortality such as age, cigarette smoking, and occupational exposure is greatly reduced in a time–series study because the distribution of these factors is not expected to vary from day to day.

In this study, we used data from stationary pollutant monitors rather than personal exposure measurements. Stationary monitoring data are inherently relevant because efforts to control the adverse effects of air pollution usually depend upon observation and control of ambient, rather than personal, exposure. Nevertheless, potential discrepancies between personal exposures and ambient pollutant levels measured at stationary monitors are often a concern in studies of this type. The magnitude of such measurement error depends largely on the extent to which stationary monitors reflect pollutant levels throughout the study area, and on differences between outdoor and indoor exposures. Previous studies suggest that fine particle concentrations are relatively uniform within urban areas and that indoor and outdoor levels are highly correlated (*33,34*). In addition, indoor heating, air conditioning, and air filtration are rare in Mexico City, and its residents spend more time outdoors than city dwellers in the United States (*35–37*). In light of these factors, differences between area and personal exposures to fine particles are likely to be relatively minor. Moreover, because all deaths on any given day are grouped and assigned a common exposure value, the exposure measurement error is essentially of the Berkson type, which does not bias observed exposure–response relationships if it is nondifferential with respect to disease occurrence (*38*).

Despite some limitations in the data and the design of the study, our findings are relevant for public health and air pollution control. They suggest that urban air pollution at current levels leads to excess mortality and that these effects are present in large cities in developing countries as well as in Europe and North America. Fine particles may themselves cause death, or they may be a marker for some combination of air pollutants that leads to excess mortality.

References and Notes

1. U.S. EPA. Air Quality Criteria for Particulate Matter. EPA/600/P-95/001cF. Washington DC:U.S. Environmental Protection Agency, Office of Research and Development, 1996.
2. Thurston GD. A critical review of PM_{10}-mortality time–series studies. J Expo Anal Environ Epidemiol 6:3–21 (1996).
3. Ostro B. The association of air pollution and mortality: examining the case for inference. Arch Environ Health 48:337–342 (1993).
4. Schwartz J. Air pollution and daily mortality: a review and meta-analysis. Environ Res 64:36–52 (1994).
5. Dockery DW, Pope CA III. Acute respiratory effects of particulate air pollution. Annu Rev Public Health 15:107–132 (1994).
6. Schwartz J. What are people dying of on high pollution days? Environ Res 64:26–35 (1994).
7. Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE. An association between air pollution and mortality in six US cities. N Engl J Med 329:1753–1759 (1993).
8. Pope CA III, Thun MJ, Namboodiri MM, Dockery DW, Evans JS, Speizer FE, Heath CW Jr. Particulate air pollution as a predictor of mortality in a prospective study of US adults. Am J Respir Crit Care Med 151:669–674 (1995).
9. Schwartz J, Dockery DW, Neas LM. Is daily mortality associated specifically with fine particles? J Air Waste Manag Assoc 46:927–939 (1997).
10. Departamento del Distrito Federal. Programa para Mejorar la Calidad del Aire en el Valle de México, 1995–2000. Mexico City:Secretaría de Medio Ambiente del Departamento del Distrito Federal, 1996.
11. Borja-Aburto VH, Loomis DP, Shy CM, Bangdiwala SI, Rascon-Pacheco RA. Ozone, suspended particulates, and daily mortality in Mexico City. Am J Epidemiol 145:258–268 (1997).
12. Castillejos M, Gold DR, Damokosh AI, Serrano P, Allen G, McDonnell WF, Dockery D, Ruiz Velasco S, Hernández M, Hayes C. Acute effects of ozone on the pulmonary function of exercising schoolchildren from Mexico City. Am J Respir Crit Care Med 152:1501–1507 (1995).
13. Hastie TJ, Tibshirani RJ. Generalized Additive Models. New York:Chapman, Hall, 1990.
14. Schwartz J. Air pollution and hospital admissions for respiratory disease. Epidemiology 7:20–28 (1996).
15. Kelsall JE, Samet JM, Zeger SL, Xu J. Air pollution and mortality in Philadelphia, 1974–1988. Am J Epidemiol 146:750–762 (1997).
16. Cleveland WS, Devlin SJ. Robust locally-weighted regression and smoothing scatterplots. J Am Stat Assoc 74:829–836 (1988).
17. McCullagh P, Nelder JA. Generalized Linear Models. New York:Chapman and Hall, 1989.
18. Verhoeff AP, Hoek G, Schwartz J, van Wijnen JH. Air pollution and daily mortality in Amsterdam. Epidemiology 7:225–230 (1996).
19. Pönkä A. Asthma and low level air pollution in Helsinki. Arch Environ Health 46:262–270 (1991).
20. Kinney PL, Özkaynak H. Associations of daily mortality and air pollution in Los Angeles County. Environ Res 54:99–120 (1991).
21. Rothman KJ. Induction and latent periods. Am J Epidemiol 14:253–259 (1981).
22. Loomis DP, Borja-Aburto VH, Bangdiwala SI, Shy CM. Ozone and Daily Mortality in Mexico City: A Time–Series Analysis. Research Rpt 75. Cambridge, MA:Health Effects Institute, 1996.
23. Kinney PL, Ito K, Thurston GD. A sensitivity analysis of mortality/PM-10 associations in Los Angeles. Inhal Toxicol 7:59–69 (1995).
24. Kalkstein LS. A new approach to evaluate the impact of climate on human mortality. Environ Health Perspect 96:145–150 (1991).
25. Ostro B, Sanchez JM, Aranda C, Eskeland GS. Air pollution and mortality: results from a study of Santiago, Chile. J Expo Anal Environ Epidemiol 6:97–114 (1996).
26. Saldiva PHN, Pope CA III, Schwartz J, Dockery DW, Lichtenfels AJ, Salge JM, Barone I, Böhm GM. Air pollution and mortality in elderly people: a time–series study in Sao Paulo, Brazil. Arch Environ Health 50:159–163 (1995).
27. Ito K, Thurston GD. Daily PM10/mortality associations: an investigation of at risk populations. J Expo Anal Environ Epidemiol 6:79–95 (1996).
28. Touloumi G, Katsoutanni K, Zmirou D, Schwartz J, Spix C, Ponce de Leon A, Tobias A, Quennel P, Rabczenko D, Bacharova L, et al. Short-term effects of ambient oxidant exposure on mortality: a combined analysis within the APHEA project. Am J Epidemiol 146:177–185 (1997).
29. Verhoef AP, Hoek G, Schwartz J, van Wijnen JH. Air Pollution and daily mortality in Amsterdam. Epidemiology 7:225–230 (1996).
30. Hoek G, Schwartz JD, Groot B, Eilers P. Effects of

ambient particulate and ozone on daily mortality in Rotterdam, the Netherlands. Arch Environ Health 52:455–463 (1997).
31. Anderson HR, Ponce de Leon A, Bland JM, Bower JS, Strachan DP. Air pollution and daily mortality in London: 1987–92. Br Med J 312:665–669 (1996).
32. Simpson RW, Williams G, Petroeschevsky A, Morgan G, Rutherford S. Associations between outdoor air pollutants and daily mortality in Brisbane, Australia. Arch Environ Health 52:442–454 (1997).
33. Dockery DW, Spengler JD. Indoor–outdoor relationships of respirable sulfates and particulates. Atmos Environ 15:335–343 (1981).
34. Suh HH, Spengler JD, Koutrakis P. Personal exposures to acid aerosols and ammonia. Environ Sci Tech 26:2507–2517 (1992).
35. Rojas-Bracho L. Evaluación del Grado de Exposición a Aeropartículas en los Habitantes de la Zona Metropolitana de la Ciudad de México [Master's thesis]. Universidad Nacional Autónoma de México, Mexico City, 1994.
36. Fernández-Bremauntz A, Quentin MJ. A survey of commuter travel habits in the metropolitan area of Mexico City. J Expo Anal Environ Epidemiol 2(suppl 2):1–17 (1992).
37. Freeman NCG, Waldman JM, Lioy PJ. Design and evaluation of a location and activity log used for assessing personal exposure to air pollutants. J Expo Anal Environ Epidemiol 1:327–338 (1991).
38. Armstrong BG. The effects of measurement error on relative risk regressions. Am J Epidemiol 132:1176–1184 (1990).