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Do associations between airborne particles and daily mortality in Mexico City differ by measurement method, region, or modeling strategy?

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We evaluated whether associations between PM_{10} and daily mortality in Mexico City differ by the PM_{10} measurement device or by regional differences in particle composition. Additionally, we reanalyzed previously collected data in light of recent insights about flaws in commonly used time series analysis techniques. We examined daily associations between mortality and four indicators of ambient PM_{10} using Poisson regression, controlling for temperature and time trends with cubic natural splines. Associations were calculated for five subregions corresponding to five monitoring sites and pooled for the entire metropolitan area. PM_{10} was measured with three methods: Tapered Element Oscillating Microbalance (TEOM), Sierra–Anderson High Volume (Hi-Vol) and Harvard Impactor (HI), the latter only at one site. In addition, predicted values of daily PM_{10} were developed using the Hi-Vol measurements, which were taken every sixth day, and weather, visibility and other pollutant data. We assigned deaths to the exposure from the monitor nearest to their residence. We also re-evaluated the HI $PM_{2.5}$ and mortality association in southwest Mexico City, which was estimated previously using nonparametric statistical models. Slight decreases in effect estimates were observed (a 1.45% increase (95% CI: 0.09%, 2.83%) in total mortality per 10 $\mu g/m^3$ increment of $PM_{2.5}$ at lag 0) compared to a 1.68% change (95% CI: 0.45%, 2.93%) using the previously employed nonparametric approach. Using data pooled over all the regions, PM_{10} measured by the TEOM and the predicted PM_{10} values showed little association with mortality at any of the lags examined. The pooled estimates for Hi-Vol PM_{10} (using one sixth of the data) were positive across all lags examined and significant for lags 3 and 5. No consistent patterns of differing associations were seen across regions that would correspond with particle toxicity or composition. Particulate air pollution, measured with gravimetric methods, is associated with daily mortality and presents a risk to health in Mexico City. The reanalysis suggests that previous research is robust to statistical method and likely to yield the same overall conclusions about the short-term effects of airborne particles on mortality.
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Introduction

Airborne particles of less than 10 μg aerodynamic diameter (PM_{10}) are of concern for health, as they can deposit in the lower airways and gas-exchanging portions of the lung. For epidemiological research, exposure to these particles is frequently assigned based on measurements from outdoor monitors. Recent studies on ambient particle pollution and daily mortality have revealed consistent effect estimates from a variety of settings (Ostro, 1993; Dockery and Pope, 1994; Schwartz, 1994; Thurston, 1996; Ostro et al., 1996; Borja-Aburto et al., 1997; Borja-Aburto et al., 1998; Loomis et al., 1999; Castillejos et al., 2000; Samet et al., 2000a; Tellez-Rojo et al., 2000). Few reports, however, have addressed the differences that the PM_{10} measurement technique may make in epidemiologic effect estimates. Although some studies have examined comparability of PM_{10} measurement methods, the focus has not been on the associations with health outcomes (Allen et al., 1997; O'Neill et al., 2002).

An additional question of interest is which physicochemical characteristics of particulate matter are responsible for health effects observed in toxicology, controlled exposure, and epidemiology studies (NRC, 1998; Dominici et al., 2003). Researchers are beginning to address this question; in one study, combustion-source particles were associated with daily mortality in six US cities, but crustal source particles were not (Laden et al., 2000). In metropolitan Mexico City, several research efforts

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have characterized regional variation in particle composition and assessed relative toxicities of these particles (Bonner et al., 1998; Alfaro-Moreno et al., 2002; Chow et al., 2002).

Finally, recent methodological advances in the field of air pollution epidemiology have raised questions about whether previous estimates of the associations between air pollution and daily mortality are biased (Dominici et al., 2002; Samet et al., 2003). Since several previous studies conducted in Mexico City have used methods that have since been called into question, application of corrected methods to data from this region can provide insights into whether the associations previously reported are robust to analytical approach.

The present study has three goals: (1) to evaluate different PM_{10} metrics and their relationship with daily mortality in Mexico City; (2) to determine whether differences in the associations in different zones of the city exist that are consistent with previously observed variations in toxicity and composition of the particles; and (3) to evaluate sensitivity of results to the choice of modeling strategy.

Methods

Study Area

Mexico City is one of the world's largest urban areas and its pollution problems have received substantial attention from researchers and policymakers in recent years (Molina and Molina, 2002). The metropolitan area of Mexico City includes 16 counties of the Federal District and 27 counties of the State of Mexico, with a population of approximately 20 million (INEGI/DDF, 1999). The valley where Mexico City is located covers about 7500 km^2 and is 2240 m above sea level. The surrounding mountains, prevailing winds, altitude, and winter thermal inversions facilitate increased pollutant concentrations in this densely populated region.

Air Pollution Data

Data from three different PM_{10} metrics were available for comparisons: two from the government of Mexico City (one with daily concentrations, one with every sixth day measures, from 1994 to 1998), and one PM_{10} metric from an academic research effort (daily concentrations in 1994 and 1995). In a previous analysis (O'Neill et al., 2002), we found low correlations between the two methods used by the Mexico City government to measure and regulate PM_{10}, as well as between one of the government methods and the research group's data. We also found large variation in the mean levels measured by the two government methods, depending on the monitoring site (O'Neill et al., 2002). We speculated that the observed differences could be important for epidemiology studies of the health impacts of particulate air pollution. In the current study, we report results from separate time series analyses of mortality and PM_{10} using these three metrics, as well as a series estimated from the PM_{10} data sampled every sixth day. We include comparisons between the metrics as well as among the five regions of Mexico City corresponding to both the principal monitoring sites and previous evaluations of differences in particle composition and toxicities.

The Mexico City government measures PM_{10} with two different technologies: the Sierra–Anderson PM_{10} High Volume Air Sampler System (Hi-Vol), operated every sixth day, and the Rupprecht & Patashnik Tapered Element Oscillating Microbalance sampler (TEOM), which takes measurements continuously. The TEOM method allows estimation of particle concentration by recording the frequency of oscillations of a glass rod, which vary according to the mass of particles on a heated filter on top of this rod (Patashnick and Rupprecht, 1991). The Hi-Vol method takes 24-h integrated samples of particles by pumping air past a filter mounted behind a size-selective inlet, and the filter is then weighed in a climate-controlled room (Chow, 1995). Five stations of the Mexico City monitoring network (Figure 1) had observations for both measurement methods for 1994–1998. The data sets were provided by Roberto Muñoz (Secretaría del Medio Ambiente, Gobierno del Distrito Federal) and Jorge Martinez (Instituto Nacional de Ecología, México) and processed at the Centro Nacional de Salud Ambiental, Metepec, Estado de México. In addition, PM_{10} measurements using Harvard Impactor (HI) low-flow size-fractionated particle samplers from the Pedregal monitor site (Figure 1) were available for 1994–July 1995. More details on this last data set are given elsewhere (Loomis et al., 1999).

For the purpose of this paper, we refer to the three PM_{10} measures being evaluated by the abbreviations Hi-Vol, TEOM, and HI. To estimate PM_{10} measured with the Hi-Vol sampler in the intervals between each sixth day, we fit linear regression models with airport visual range measurements, meteorological data, and other air pollutants (O'Neill et al., 2002). We refer to this time series of estimated PM_{10} as 'Predicted'.

In modeling the association between PM_{10} and mortality, we did not include other pollutants as covariates. Ozone is positively correlated with PM_{10} in Mexico City, and we

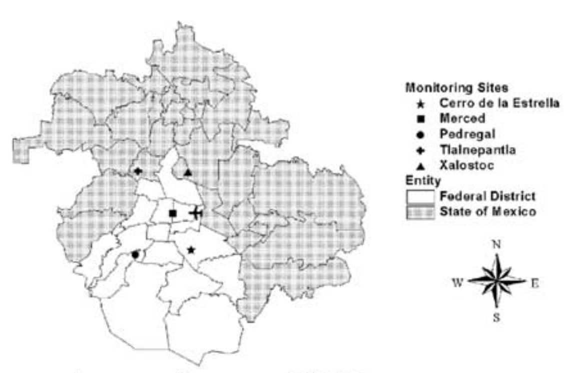

Figure 1. Mexico City metropolitan area.

wished to avoid problems with collinearity in the models. However, it is worth acknowledging that, because of this collinearity, and because of the fact that people are exposed to a mixture of pollutants, it may be difficult to separate out the distinct effects of the individual pollutants. Nevertheless, we decided to model PM_{10} alone, as previous studies in Mexico City examined the sensitivity of estimated particle associations to inclusion of other pollutants (Borja-Aburto et al., 1997; Loomis et al., 1999; Castillejos et al., 2000) and our main interest was in exploring differences across regions within the city. The previous studies found that other gaseous pollutants either occurred at very low levels (sulfur dioxide) or did not substantially change the particle effect when included in the mortality models (nitrogen dioxide).

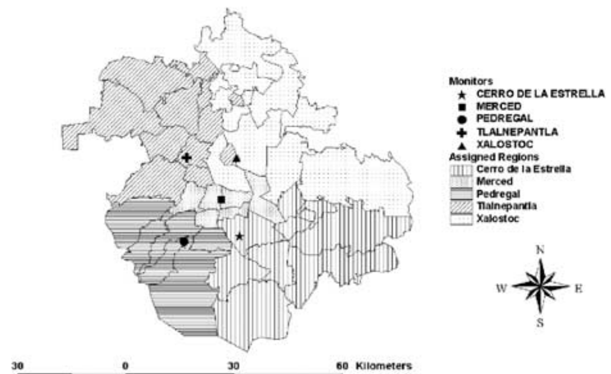

Figure 2. Regional Divisions, 1996–1998.

Mortality Data

We acquired electronic records of death certificates for 1994–1998 from the Instituto Nacional de Estadística, Geografía e Informática (INEGI). The analysis data set included individuals who both lived and died within the study area, and eliminated those who died from external causes (injuries, poisoning). After these exclusions, 324, 853 deaths occurring from January 1, 1994 to December 30, 1998 were available.

Divisions of the Mexico City Study Area

To evaluate whether the association between PM_{10} and mortality differed depending on the PM_{10} monitoring site, we assigned decedents into five regions corresponding to each of the monitors, based on the county listed on the death certificate. The county was not recorded for most residents of the Federal District in 1994 and 1995. Therefore, region-specific associations for all five regions could be evaluated only for 1996–1998. We did, however, use mortality data from a previous study to evaluate the PM_{10} association for decedents from six counties near the Pedregal monitor, for 1994 through July 31, 1995 (Borja-Aburto et al., 1998).

We assigned exposure for 1996–1998 using a digitized map. The Spatial Analyst proximity analysis feature of ArcView GIS 3.2 (Environmental Systems Research Institute, Inc.) was used to divide the map into five regions encompassing the areas nearest to each of the five monitors. Next, counties were assigned to one of the five monitor regions if their centroids, calculated by a polygon center of mass program (Esteve-Ciudad, 2000), were located within the corresponding dividing lines. Three counties are divided into two noncontiguous portions, and were therefore assigned to a region based on the majority of the area being closer to one of the monitors.

Figure 2 shows the five regional divisions for the years 1996–1998.

Weather Parameters

Previous research suggests that temperature is the principal meteorological parameter predicting mortality in Mexico City (Borja-Aburto et al., 1997; Loomis et al., 1999). The mean, minimum, and maximum daily temperature and relative humidity data, averaged from the three to 12 monitors reporting on any given day, were obtained from the Mexico City monitoring network. The network uses automatic recording instruments.

Statistical Models

First, the mortality, air pollution, and weather parameter distributions were examined individually with descriptive statistics and time-series plots. The predictors evaluated in developing the statistical models were time (in days), minimum, maximum and mean temperature and relative humidity, day of week, and season (rainy, that is June–September, vs. dry). The temperature and relative humidity values on the day of death and lagged up to 5 days, as well as 3-day moving averages with lags of zero to 2 days, were considered. Correlations between these predictor variables were evaluated to assess potential for collinearity.

To model the association between particles and daily mortality, we used Poisson regression, with daily mortality counts for each of the five regions as the dependent variable. For each region, we controlled for long-term time trends in mortality by modeling time (an integer value for the day of the time series) with a natural cubic spline (Hastie and Tibshirani, 1990; Wypij, 1996). This type of spline fits separate polynomial functions to ranges of a predictor, which are constrained to meet the boundary points (called knots) between the regions, and fits linear functions after the knots on each end of the spline (Hastie and Tibshirani, 1990; Wypij, 1996). These fully parametric models have been recommended for use in time-series analysis in light of recently discovered limitations in previous nonparametric approaches (HEI, 2003; Ramsay et al., 2003).

To choose the spline degrees of freedom, we considered both model fit using Akaike's Information Criterion (AIC) (Akaike, 1973), an indicator of model deviance penalized for the number of parameters (Hastie and Tibshirani, 1990) and plausibility of time-related effects. We examined the partial autocorrelation function, to check if the spline had reduced the residuals to a random pattern, but not induced excessive negative serial autocorrelation in the data. We selected the degrees of freedom for the natural spline of time separately for each regional model. S-Plus 2000 (Mathsoft, Inc., Seattle, WA, USA) software was used to fit all the models, using a more stringent convergence criterion than provided as the default (Dominici et al., 2002).

The other predictors were evaluated by adding them singly into a model of daily death counts; those that improved fit the most were retained. This testing was conducted on mortality data from the entire region so as to have the same set of predictors for the region-specific models. The continuous particulate matter variables (in μg/m^3) were incorporated into the models as linear terms, for lags 0–5, and the average of lags 0–5 for those metrics for which daily data were available. Models for the five regional subdivisions were fit using the same base model terms; the only predictors that varied among these models were PM_{10}, which differed by metric as well as the monitor being used, and degrees of freedom in the natural spline for controlling long-term mortality trends.

Mortality rate ratios and standard errors were calculated from the particle parameter estimate and its standard error. We adjusted the variance of the regression coefficients for any over- or underdispersion (McCullagh and Nelder, 1989). The rate ratios were expressed in terms of a 10 μg/m^3 change in concentration of PM_{10} and the corresponding 95% confidence interval (CI).

To obtain a pooled estimate of the association across all five regions, we applied a random effects model that combines the region-specific coefficients $\hat{\beta}$, using the maximum likelihood method of Berkey and co-workers (Berkey et al., 1995). The assumption of the model is that:

$$\hat{\beta}_i \sim N(\hat{\beta}, \hat{S}_i + D)$$

where $\hat{\beta}_i$ is the particle coefficient in region i, $\hat{\beta}$ is the summary estimate from all the regions, $\hat{S}_i$ is the estimated variance in region i, and D is the random variance component, reflecting heterogeneity among the five regions.

In light of recent issues that have been raised about the methods used to analyze time-series data (HEI, 2003; Samet et al., 2003), and the fact that previous publications on particles and mortality in Mexico City (Borja-Aburto et al., 1998; Loomis et al., 1999; Castillejos et al., 2000) used the loess smoothing algorithm (Cleveland and Devlin, 1988) and default convergence criteria, we also conducted a sensitivity analysis comparing model specifications at different lags, using $PM_{2.5}$ data from the same region (Pedregal) for which effects were previously reported (Borja-Aburto et al., 1998). Specifically, we compared results using models that used the Splus default model convergence criterion and the loess smoothers for time and weather variables, with the results using the parametric modeling methods described above. Finally, as recommended in a recent report (HEI, 2003), we evaluated the sensitivity of our results obtained from the parametric models to the degrees of freedom chosen for the natural spline of time.

Results

Mortality models

The final parameters for the mortality models included natural splines for time with degrees of freedom fit separately for each region using criteria described previously, and a natural spline for the 3-day average of minimum temperature (lags 0–2), with 4 degrees of freedom. Linear terms for particles were included individually in separate models for lags 0–5, and the average of lags 0–5 where daily data were available.

Descriptive Statistics

Total mortality for each of the regions ranged from just under 30,000 for Pedregal during 1996–1998, to almost 60,000 for the Merced region (Table 1). During this time period, particle levels were highest at the Xalostoc monitor and lowest in Pedregal, the southwest part of the city. (Table 1) The 3-day average minimum temperature never dipped below 1.2°C for the study period. The 3-day average minimum temperature was included in the models for all the regions, but we report it only once in the table for each time period to avoid repetition. Particle levels showed seasonal variation in time-series plots, with levels generally higher in the winter. Mortality showed strong winter peaks and increased over the study period.

As reported previously (O'Neill et al., 2002), PM_{10} levels measured at the same monitoring sites using different methods were not well correlated with each other. The highest correlation between TEOM and Hi-Vol measures was seen at the Pedregal monitor in 1994 and 1995 (0.72), but the other correlations ranged from 0.43 to 0.64. The highest correlation among any particle metrics (0.90) was observed between the Hi-Vol and the HI for PM_{10} at Pedregal.

Particle effects

Associations between PM_{10} and daily mortality for the TEOM, predicted, and HI PM_{10} metrics are presented in Table 2. The pooled estimates for the predicted PM_{10} series were all nonsignificant and negative at all but one lag; the point estimate for the average of lags 0–5 suggested no association with mortality. The pooled TEOM measures of PM_{10} were also all not significant and point estimates were negative at all lags except one. The point estimate accounting for exposure on the day of death and five preceding days was a 0.05% increase in mortality per 10 μg/m^3 increase in PM_{10} (95% CI, −0.25%, 0.35%). By region, the TEOM point

Table 1. Descriptive statistics for air pollution (unlagged, single day values), temperature, and mortality data by monitor, corresponding residence region, and date for Mexico City.

Monitor/region dates	Parameter	Days with observations	Total	Mean	Standard deviation	Minimum	Maximum
Xalostoc	Daily deaths	1095	42,255	38.6	8.4	19	70
1996–1998	PM_{10} Hi-Vol[a]	165		164.0	68.5	40.0	335.0
	PM_{10} TEOM[b]	1095		107.5	54.1	16.5	291.2
	PM_{10} predicted[c]	1051		162.4	45.9	60.6	320.0
	Min. temp °C[d]	1095		10.8	3.2	1.1	18.5
Tlalnepantla	Daily deaths	1095	39,254	35.9	8.0	17	70
1996–1998	PM_{10} Hi-Vol	171		79.6	39.8	25.0	264.0
	PM_{10} TEOM	1095		71.1	40.4	10.4	275.9
	PM_{10} predicted	1051		84.2	27.4	17.7	175.0
Merced	Daily deaths	1095	58,178	53.1	10.5	25	96
1996–1998	PM_{10} Hi-Vol	171		75.3	37.7	17.0	266.0
	PM_{10} TEOM	1095		80.3	41.0	9.4	318.7
	PM_{10} predicted	1051		75.4	26.9	12.3	160.8
Cerro de la Estrella	Daily Deaths	1095	36,778	33.6	7.4	17	63
1996–1998	PM_{10} Hi-Vol	168		69.5	45.8	15.0	292.0
	PM_{10} TEOM	1095		68.6	35.5	13.7	268.3
	PM_{10} Predicted	1038		77.9	26.9	11.2	154.4
Pedregal	Daily deaths	1095	29,454	26.9	6.4	9	52
1996–1998	PM_{10} Hi-Vol	169		46.3	28.3	5.0	226.0
	PM_{10} TEOM	1095		51.6	31.7	7.8	264.4
	PM_{10} predicted	1051		30.2	12.3	-0.5	86.3
Pedregal	Daily deaths	577	18,415	31.9	6.4	16	55
1994–July 31, 1995	PM_{10} Hi-Vol	85		59.5	21.0	24.0	114.0
	PM_{10} TEOM	549		48.2	20.4	8.7	152.5
	Impactor PM_{10}[e]	538		58.4	21.1	15.0	154.0
	PM_{10} predicted	563		31.4	11.6	3.9	75.9
	Min. temp°C	577		10.9	2.2	3.3	16.1

[a]PM_{10} measured by Sierra-Anderson PM_{10} High Volume Air Sampler System, 24 h mean in $\mu g/m^3$.
[b]PM_{10} measured by Rupprecht & Patashnik Tapered Element Oscillating Microbalance sampler.
[c]PM_{10} values predicted from Hi-Vol and other air pollution, meteorology data.
[d]The 3-day (lags 0,1,2) mean of average minimum daily temperature from Mexico City monitoring network.
[e]PM_{10} measured by Harvard Impactor low-flow size-fractionated particle sampler.

estimates were positive for all lags at the Cerro de la Estrella monitor, and the estimate considering lags 0–5 was a 0.65% increase in mortality per 10 $\mu g/m^3$ increase in PM_{10} (95% CI, 0.01%, 1.30%). For the remainder of the regions, the TEOM metric showed no consistent patterns and no significant associations with mortality. Similarly, for the predicted PM_{10} series, no consistent patterns were observed, although the point estimates were positive for all but two lags in the Tlalnepantla region, where the only positive point estimate for lags 0–5 of any of the regions for this metric (0.55%, 95% CI, −0.36%, 1.47%) was seen. The only significant association for predicted PM_{10} was a negative one at lag 2 for the Pedregal monitor (−1.54%, 95% CI, −2.85%, −0.22%). In the Pedregal region, the HI PM_{10} associations for 1994–1995 were not significantly different from the other two metrics. All three metrics showed positive point estimates at lags 0 and 4, and negative point estimates at lag 2 and the average of lags 0–5.

Table 3 shows the results with the Hi-Vol metric, presented separately because these models were fitted with approximately one-sixth the data used for the models in Table 2. For this metric, the pooled analysis showed positive associations with mortality at all five lags examined that were significant at lags 3 and 5. By region, the highest point estimates were observed at lag 3 for Tlalnepantla and at lag 5 for Pedregal; the majority of the point estimates and also all of the pooled estimates were positive. We also evaluated the TEOM PM_{10} metric for these same days and the same covariate specifications. For the pooled estimates, half of the lags showed positive point estimates, and half negative, and none were significant (results not shown).

Table 4 shows the results of the sensitivity analysis using $PM_{2.5}$ data in the Pedregal region from 1994–1995. The point estimates obtained with the nonparametric model were consistently smaller than those using the default approach employed in previously published studies. When comparing the level of smoothing for time trend, for most of the lags, the intermediate degree of smoothing (5 df) also resulted in point estimates between the lesser (2 df) and greater (10 df) degrees.

Table 2. Percent change in daily mortality and 95% confidence intervals associated with 10 $\mu g/m^3$ increase in PM_{10}, 24 h mean, estimated in three different ways, pooled and by region for metropolitan Mexico City (1996–1998 and 1994–July 1995). Estimates control for time trend and minimum temperature averaged over lags 1, 2, and 3; n = days available for analysis in each region by lag.

Region	Metric	Lag 0		Lag 1		Lag 2		Lag 3		Lag 4		Lag 5		Lags 0–5	
Pooled[a]	TEOM[b]	0.04	(−0.12, 0.20)	−0.02	(−0.18, 0.13)	−0.01	(−0.27, 0.25)	−0.03	(−0.19, 0.13)	−0.03	(−0.19,0.13)	−0.05	(−0.21, 0.11)	0.05	(−0.25, 0.35)
	Predicted[c]	−0.05	(−0.29, 0.19)	0.09	(−0.16, 0.34)	−0.12	(−0.43, 0.20)	−0.02	(−0.26, 0.21)	−0.14	(−0.37,0.09)	−0.05	(−0.28, 0.18)	0.00	(−0.39, 0.38)
Xalostoc[a]	TEOM	0.08	(−0.16, 0.33)	−0.02	(−0.26, 0.23)	−0.15	(−0.40, 0.09)	−0.09	(−0.34, 0.16)	0.03	(−0.21,0.28)	0.04	(−0.21, 0.29)	0.00	(−0.40, 0.39)
	Predicted	−0.11	(−0.50, 0.27)	−0.03	(−0.41, 0.36)	−0.02	(−0.40, 0.35)	0.1	(−0.25, 0.46)	−0.13	(−0.48,0.22)	0.08	(−0.28, 0.43)	−0.09	(−0.69, 0.51)
	n	1051		1050		1049		1048		1047		1046		910	
Tlalnepantla[a]	TEOM	0.13	(−0.30, 0.57)	−0.13	(−0.57, 0.31)	−0.01	(−0.45, 0.43)	−0.12	(−0.55, 0.32)	−0.05	(−0.49,0.39)	−0.23	(−0.66, 0.20)	0.19	(−0.50, 0.88)
	Predicted	0.19	(−0.36, 0.75)	0.43	(−0.11, 0.98)	0.03	(−0.51, 0.57)	0.02	(−0.52, 0.56)	−0.24	(−0.78,0.31)	−0.01	(−0.55, 0.53)	0.55	(−0.36, 1.47)
	n	1051		1050		1049		1048		1047		1046		910	
Merced[a]	TEOM	−0.09	(−0.42, 0.24)	−0.09	(−0.42, 0.24)	−0.17	(−0.50, 0.16)	−0.04	(−0.36, 0.29)	−0.13	(−0.45,0.20)	−0.20	(−0.53, 0.12)	−0.30	(−0.83, 0.24)
	Predicted	−0.01	(−0.53, 0.51)	0.25	(−0.25, 0.76)	0.15	(−0.35, 0.65)	−0.11	(−0.60, 0.39)	−0.23	(−0.72,0.26)	−0.22	(−0.71, 0.28)	−0.06	(−0.87, 0.75)
	n	1051		1050		1049		1048		1047		1046		910	
Cerro de la Estrella[a]	TEOM	0.18	(−0.24, 0.61)	0.12	(−0.31, 0.55)	0.58	(0.16, 1.01)	0.35	(−0.08, 0.77)	0.18	(−0.25,0.60)	0.10	(−0.32, 0.53)	0.65	(0.01, 1.30)
	Predicted	−0.22	(−0.83, 0.39)	−0.34	(−0.95, 0.27)	−0.37	(−0.98, 0.24)	−0.15	(−0.75, 0.45)	0.1	(−0.51,0.72)	−0.18	(−0.79, 0.43)	−0.09	(−1.01, 0.85)
	n	1038		1037		1036		1035		1034		1033		862	
Pedregal[a]	TEOM	−0.16	(−0.71, 0.39)	0.03	(−0.52, 0.59)	−0.24	(−0.79, 0.31)	−0.23	(−0.78, 0.33)	−0.38	(−0.93,0.18)	0.00	(−0.56, 0.56)	−0.17	(−0.93, 0.60)
	Predicted	−0.14	(−1.48, 1.22)	0.21	(−1.11, 1.56)	−1.54	(−2.85, −0.22)	−0.8	(−2.13, 0.54)	−0.31	(−1.65,1.05)	−0.12	(−1.47, 1.25)	−1.24	(−3.42, 0.99)
	n	1051		1050		1049		1048		1047		1046		910	
Pedregal[d]	TEOM	0.11	(−0.75, 0.98)	0.18	(−0.67, 1.04)	−0.58	(−1.43, 0.28)	0.21	(−0.67, 1.10)	0.15	(−0.73,1.05)	0.04	(−0.85, 0.94)	−0.17	(−2.16, 1.86)
	Predicted	0.6	(−1.12, 2.35)	0.45	(−1.26, 2.18)	−0.88	(−2.60, 0.86)	−1.29	(−3.08, 0.54)	0.38	(−1.45,2.24)	−0.90	(−2.69, 0.93)	−0.09	(−4.30, 4.30)
	Impactor[e]	0.89	(−0.11, 1.90)	−0.52	(−1.50, 0.48)	−0.51	(−1.55, 0.54)	−0.58	(−1.62, 0.47)	0.57	(−0.47,1.62)	0.51	(−0.51, 1.55)	−0.02	(−2.14, 2.14)
	n	501		501		500		499		498		497		306	

[a] Estimates for 1996–1998.
[b] PM_{10} measured by Rupprecht & Patashnik Tapered Element Oscillating Microbalance sampler.
[c] PM_{10} estimated from Sierra-Anderson PM_{10} High Volume Air Sampler System measures, visibility, weather, and other pollution data.
[d] Estimates for 1994–July 1995.
[e] PM_{10} measured by Harvard Impactor low-flow size-fractionated particle sampler.

Table 3. Percent change in daily mortality and 95% confidence intervals associated with 10 $\mu g/m^3$ increase in PM_{10}, measured with Sierra-Anderson High Volume Air Sampler System, 24 h mean, every sixth day, pooled and by region for metropolitan Mexico City (1996–1998).

Lag	Pooled (all five regions) $n = 171$, df = 5	Xalostoc $n = 171$, df = 5	Tlalnepantla $n = 171$, df = 5	Merced $n = 171$, df = 5	Cerro de la Estrella $n = 171$, df = 5	Pedregal $n = 171$, df = 5
0	0.02 (−0.29, 0.32)	−0.01 (−0.50, 0.47)	0.20 (−0.68, 1.09)	0.16 (−0.51, 0.83)	−0.39 (−1.10, 0.32)	0.47 (−0.64, 1.59)
1	0.13 (−0.27, 0.54)	0.58 (0.09, 1.07)	0.15 (−0.64, 0.95)	−0.25 (−0.95, 0.45)	−0.35 (−1.08, 0.38)	0.51 (−0.68, 1.72)
2	0.21 (−0.10, 0.52)	0.34 (−0.15, 0.84)	0.17 (−0.64, 0.98)	0.03 (−0.62, 0.68)	0.36 (−0.40, 1.13)	−0.31 (−1.50, 0.89)
3	0.53 (0.07, 0.99)	0.51 (−0.04, 1.07)	1.39 (0.64, 2.16)	0.34 (−0.36, 1.05)	−0.09 (−0.87, 0.70)	0.45 (−0.68, 1.60)
4	0.11 (−0.20, 0.41)	0.09 (−0.37, 0.56)	0.28 (−0.47, 1.03)	0.14 (−0.58, 0.86)	−0.10 (−0.87, 0.68)	0.14 (−1.05, 1.35)
5	0.38 (0.07, 0.70)	0.35 (−0.13, 0.84)	0.43 (−0.42, 1.30)	0.41 (−0.28, 1.10)	0.02 (−0.71, 0.75)	1.38 (0.17, 2.60)

Estimates control for time trend and minimum temperature averaged over lags 1, 2, and 3 using natural cubic splines; number of days available for analysis in each region listed as n. All temperature splines used 4 degrees of freedom (DF); seasonal spline df listed after n.

Table 4. Sensitivity to modeling method (generalized additive model (GAM) vs. parametric) and degrees of freedom (df) for time trend.

Lag	GAM: 2 loess terms, default convergence[a]	Parametric: cubic natural splines[b], varying df's for time trend		
		5 df	10 df	2 df
0	1.68 (0.45, 2.93)	1.45 (0.09, 2.83)	1.60 (0.20, 3.02)	1.79 (0.48, 3.11)
1	−0.36 (−1.56, 0.86)	−0.71 (−2.06, 0.67)	−0.80 (−2.18, 0.60)	−0.09 (−1.38, 1.22)
2	−0.21 (−1.40, 1.00)	−0.59 (−1.95, 0.79)	−0.73 (−2.11, 0.68)	0.10 (−1.18, 1.40)
3	−0.18 (−1.40, 1.05)	−0.70 (−2.09, 0.71)	−1.05 (−2.49, 0.40)	0.20 (−1.10, 1.52)
4	1.31 (0.08, 2.55)	0.92 (−0.46, 2.32)	0.64 (−0.79, 2.10)	1.60 (0.30, 2.91)
5	1.49 (0.25, 2.73)	1.17 (−0.19, 2.55)	1.05 (−0.36, 2.48)	1.72 (0.43, 3.04)
0–5	1.77 (−0.26, 3.83)	1.17 (−1.54, 3.95)	0.51 (−2.60, 3.71)	1.90 (−0.36, 4.21)

Results are percent change in daily mortality and 95% confidence intervals associated with a 10 $\mu g/m^3$ increase in $PM_{2.5}$ in Pedregal, 1994–July 1995, $n = 537$. Estimates control for time trend and minimum temperature averaged over lags 1, 2, and 3.
[a]Convergence precision: 10^{-3}, biased standard errors. Loess spans: 215 days for time, 269 days for temperature.
[b]Convergence precision: 10^{-14}, modeling temperature with a cubic natural spline, 4 df for all models.

Discussion

We discuss the results of this analysis in terms of the three study goals: (1) to evaluate different PM_{10} metrics and their relationship with daily mortality in Mexico City; (2) to determine whether differences in the associations in different zones of the city exist that are consistent with previously observed variations in toxicity and composition of the particles; and (3) to evaluate sensitivity of results to the choice of modeling strategy.

The first objective was to evaluate different PM_{10} metrics and their relationship with daily mortality in Mexico City. The present results are consistent with previous evidence of a small positive association between particulate matter and daily mortality in Mexico City when particles are measured with a gravimetric method. Measures of PM_{10} made by the Mexico City government with a gravimetric method (Hi-Vol), when pooled for the entire metropolitan region, had positive associations with mortality at all lags of exposure considered, and significant positive associations at lags 3 and 5. However, daily mortality was not consistently or significantly associated with PM_{10} measured with a continuous method (TEOM) or PM_{10} imputed using every-sixth-day gravimetric measures and data on other pollutants, visibility, and weather.

The lack of association with the predicted PM_{10} series may be because the covariates used to impute the exposures for days without measurements may have null or negative associations with mortality, thus pulling down the overall estimates in the mortality models. The predicted PM_{10} series can be viewed as a composite indicator of several pollutants, visibility, and meteorological parameters. However, the TEOM PM_{10} measure also did not demonstrate a pattern of positive associations when pooled for the entire region. This may be partly due to the differences in the way this measurement device works. Given previous evidence from Mexico City (O'Neill et al., 2002) that TEOM measurements are poorly correlated with gravimetric ones, it may be that the device is not measuring the biologically relevant portion of the particulate mass, or that other factors are limiting the reliability of this data as an exposure indicator. Our comparison of the TEOM association with mortality with the Hi-Vol associations, using the exact same time series and model specifications, demonstrated that the patterns in observed associations are not due to the every-sixth-day sampling selection driving the results.

The second goal of this study was to assess whether observational epidemiology results would be consistent with findings on regional variations in particle toxicity and composition in Mexico City. A recent study reports on *in vitro* biologic effects from PM_{10} measured in northern, central, and southern Mexico City during 1991 (Alfaro-Moreno et al., 2002), in zones that correspond to Xalostoc, Merced, and Pedregal, respectively. Although PM_{10} from all three locations caused DNA breakage, apoptosis, and cell death, the northern and central particles were the most toxic. Compositional analyses of PM_{10} sampled in 1993 found higher levels of bacterial lipopolysaccharide (endotoxin) in the southern part of the city, and all transition metals except lead were highest in the north and showed a decreasing north–south gradient (Bonner et al., 1998). Another analysis found a similar pattern of particle composition by geographic region, and examined the proinflammatory and cytoxic properties *in vitro* of particles sampled in northern and southeast Mexico City during spring, 2000 (Osornio-Vargas et al., 2003). Cytotoxic and proinflammatory properties of the particles differed by both location and particle size ($PM_{2.5}$ and PM_{10}), with components present in the coarse fraction of the particles ($PM_{2.5\text{-}10}$) being the main contributor to the differences in observed effects, and endotoxin (at higher concentrations in the southeast) as a major mediator of proinflammatory particle effects (Osornio-Vargas et al., 2003). In 1997, higher levels of elemental carbon and $PM_{2.5}$ ammonium sulfate were seen in the north, but $PM_{2.5}$ ammonium nitrate particles were higher in the south (Chow et al., 2002). An analysis of particles sampled during 1997 found that 40–55% of PM_{10} in Mexico City was composed of geological materials (crustal species AL, Si, Fe, Mg, and Ca), especially at the Xalostoc monitor (Edgerton et al., 1999).

Based on knowledge about particle toxicity, one might expect to see higher associations with mortality in the northern regions of the study area. However, particles in southern regions may have stronger inflammatory than cytotoxic effects due to endotoxin levels (Osornio-Vargas et al., 2003) and the role these mechanisms may play in contributing to mortality has yet to be fully elucidated. In our analysis, none of the three PM_{10} metrics evaluated by region showed consistent patterns of different associations. When evaluating the effect of PM_{10} averaged over lags 0–5, the predicted series showed a significant positive association with mortality in Tlalnepantla (0.66%, 95% CI, 0.12%–1.20%), but in the other regions the association was not significantly different from zero. The TEOM effect point estimate was highest in Cerro de la Estrella for this same averaging time (0.54%, 95% CI, 0.19%–0.89%), but again, effectively zero at the other sites. The strength of the Hi-Vol association with mortality was greatest at Tlalnepantla, for lag 3, and Pedregal for lag 5, but here again, no strong patterns consistent with the toxicology results emerged.

Other characteristics of the region may be of interest when interpreting the present findings. The topography and pollution sources of the northern part of the study area are quite distinct from the southern region. Important particle sources near the Xalostoc monitor, which is in an industrial corridor, include a smelter, a soap factory, a precement mill, and heavy diesel-run vehicular traffic on two major highways (Muñoz and Retama, personal communication, 2001). Prevailing winds bring in dust from the dried Lake Texcoco basin, which includes organic matter and possibly fecal pathogens. The topography is largely flat except for the Sierra de Guadalupe, 2 km west of the monitor. The numerous point particle sources in Xalostoc area may render data from the ambient monitor less accurate than in other areas. This is also the case for Tlalnepantla, the other northern monitor. In contrast, the southern part of the study area is characterized by residential zoning and pollution sources consisting primarily of automobile traffic, and to the south, the 3300 m high Sierra de Ajusco mountain range, which prevents dispersal of pollution. These conditions may mean that the Pedregal monitor measures a more uniform mix of particles, and is more reflective of day to day exposure.

There is limited information on how well ambient monitors reflect personal particle exposure in Mexico. Therefore, we cannot draw firm conclusions at this stage with regard to whether the inability to detect substantial between-region disparities in mortality associations relates to differential adequacy of the monitor measurements as a surrogate for personal exposure. In addition to personal exposure, there may be underlying regional differences in susceptibility, related to disease status, socioeconomic factors, or other characteristics, that may affect the estimates. Owing to power considerations and data limitations, it was not feasible to evaluate all these possible factors, but they are worth mentioning for the purpose of future potential analyses.

The third goal of this paper was to evaluate sensitivity of results to the choice of modeling strategy. To put our work in context, we begin by reviewing previously published reports. The majority of published mortality/particle associations in Mexico City are for the Pedregal subregion (January 1, 1993–July 31, 1995), using the HI measurements. One study showed a 1.4% increase in total mortality (95% CI, 0.2%–2.5%) associated with a 10 $\mu g/m^3$ increase in $PM_{2.5}$, on the day of death and 4 days previously (Borja-Aburto et al., 1998). Another study found increases in total mortality with 10 $\mu g/m^3$ increments in particles: 1.83% (95% CI, 0.01%–2.96%) for PM_{10}, 1.48% (95%CI, 0.98%–2.68%) for $PM_{2.5}$, and 4.07% (95% CI, 2.49%–5.66%) for $PM_{10\text{-}2.5}$ (Castillejos et al., 2000). Finally, a 6.9% (95% CI, 2.5%–11.3%) excess in infant mortality in the same area was observed for 10 μg/m^3 increase in $PM_{2.5}$, during the period of 3–5 days before the day of death (Loomis et al., 1999). All of these previously described studies used nonparametric methods (generalized additive models with more than one nonparametric smoother to model time trend and weather) with inadequately stringent model convergence criteria to develop the effect estimates.

Two studies using government-collected data have been published to date. One evaluated the associations of daily mortality and total suspended particles (TSP) during 1990–1992, for the Federal District, excluding one county. A 0.58% increase in total mortality (95% CI, 0.33%, 0.83%) was observed per 10 μg/m^3 increment in TSP, controlling for O_3 and sulfur dioxide (Borja-Aburto et al., 1997). If we convert the TSP estimate to PM_{10}, assuming that half of the TSP is made up of PM_{10}, the estimate is about 1.20% excess daily mortality. That study used parametric methods to model the nonlinear covariates. Another study examined respiratory-cause mortality in the Federal District for the year 1994, finding a 2.4% increase (95% CI, 0.4–4.5%) per 10 μg/m^3 increment in PM_{10}, measured with the TEOM, controlling for minimum temperature and season (Tellez-Rojo et al., 2000). That study did not specify whether Splus software was used and it was not clear if more than one nonparametric smoother was used for covariates.

The overall effect estimates we report for the government PM_{10} metrics are lower than reports from previous research in Mexico City. In part, this is because previous reports emphasize the positive, significant associations found at a particular lag, although some of the lags evaluated in these previous studies showed negative though nonsignificant effects. Additionally, due to power considerations, we evaluated all-cause, all-age mortality, and other studies evaluating susceptible subsets of decedents (e.g., infants or those dying from respiratory conditions) would be more likely to detect a stronger signal. Another possible explanation is that the quality of the exposure data we used differs from that employed in the previous analyses, either due to the measurement method used or quality control during the evaluated years.

For associations between mortality and PM_{10} measured with the Harvard Impactor at Pedregal, the models employed for the present study yielded effect estimates in the range of those reported in previously cited investigations (Table 4). We evaluated 1.5 years of data rather than 2.5 years as did the previous investigators because of difficulties in acquiring the government pollutant and mortality data for 1993. The patterns of the strongest positive associations being observed at lags 0, 4, 5, and lags 0–5 are consistent with previous modeling (Borja-Aburto et al., 1998). Additionally, our results were robust to the degree of smoothing for time trend; the effect at lag 0 was positive and significant, for every model fitted. These findings suggest that conclusions from previous studies are unlikely to change substantially, although point estimates would be expected to drop, if data are reanalyzed with new techniques. The robustness of analytical results to smoothing parameters and other modeling choices has been evaluated in numerous other regions of the world and for the most part the reduction in estimates has been marginal (Katsouyanni et al., 2002; Lin et al., 2003).

The consistency of our results with the previous ones suggests that the lower estimates we found for the government PM_{10} metrics are not entirely a result of differences in modeling strategy. Instead, a true difference in the association between PM_{10} and mortality may exist for the different metrics, regions and time periods we evaluated. It is also possible that error in the government measurements, compared to the HI data, which were taken with more rigorous quality control measures, may contribute to attenuation of the effect, and hence the difference between our results and previous studies.

Conclusions

This study compared the associations of different metrics of particulate air pollution with mortality in a time-series analysis. The point estimates for the effects of Hi-Vol and TEOM-measured particles showed no consistent pattern of differences across regions, either on a subregional basis or pooled. However, future studies comparing the two government metrics in relation to other health end points (e.g., hospital admissions), limited to particular ages or causes of death, or using a design other than the time-series approach employed here, might show different associations. Such studies could provide further insight into whether the difference in the concentrations measured by these methods or the differences in particle toxicity and composition are relevant for protecting the health of the populace.

A recent analysis of PM_{10} and mortality in 90 US cities found that some cities had no or even negative effects, and that the effect estimate for excess mortality for 20 US cities per 10 μg/m^3 of PM_{10} was about 0.5% for each 10 μg/m^3 increase in PM_{10} at lag 1 (Samet et al., 2000b). Our present findings for the government PM_{10} data are within the range of those observed in the US cities.

Although many of the results presented here do not show a strong positive association between PM_{10} and mortality in Mexico City, they should not be understood as weakening the case that air pollution presents a substantial public health burden in that populated city. Numerous epidemiological and toxicological studies, using various designs, have shown a variety of health effects from exposure to Mexico City air pollution. Furthermore, our examination of the data used for previous studies of mortality and pollution in the southwest region show that the association is relatively robust to the choice of statistical method. Additionally, several published studies of the effects of long-term exposure to air pollution suggest that the burden of living in a city (such as Mexico City) with high levels of particles can have damaging consequences to health and longevity. The present analysis contributes to knowledge of pollution and one health outcome in Mexico City, and should be interpreted along with the body of literature examining associations between health and air pollution. The issues raised in this paper highlight the challenges of evaluating these associations, and suggest the need for increasingly sophisticated and thorough analytical approaches in future research efforts.

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