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The Association between Daily Mortality and Ambient Air Particle Pollution in Montreal, Quebec

2. Cause-Specific Mortality

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This study was undertaken to determine whether variations in concentrations of particulates in the ambient air of Montreal, Quebec, during the period 1984 to 1993, were associated with daily variations in cause-specific daily mortality. Fixed-site air pollution monitors in Montreal provided daily mean levels of various measures of particles and gaseous pollutants. Total sulfate was also measured daily (1986–1993) at a monitoring station 150 km southeast of the city (Sutton, Quebec). We used coefficient of haze (COH), extinction coefficient, and sulfate from the Sutton station to predict fine particles and sulfate from fine particles for days that were missing. We estimated associations between cause-specific mortality and $PM_{2.5}$, PM_{10}, predicted fine particles and fine sulfate particles, total suspended particles, coefficient of haze, extinction coefficient, and total sulfate measured at the Sutton station. We selected a set of underlying causes of death, as recorded on the death certificates, as the endpoint and then regressed the logarithm of daily counts of cause-specific mortality on the daily mean levels for the above measures of particulates, after accounting for seasonal and subseasonal fluctuations in the mortality time series, non-Poisson dispersion, weather variables, and gaseous pollutants. We found positive and statistically significant associations between the daily measures of ambient particle mass and sulfate mass and the deaths from respiratory diseases and diabetes. The mean percentage change in daily mortality (MPC), evaluated at the interquartile range for pollutants averaged over the day of death and the preceding 2 days, for deaths from respiratory diseases was $MPC_{COH} = 6.90\%$ (95% CI: 3.69–10.21%), $MPC_{Predicted\ PM2.5} = 9.03\%$ (95% CI: 5.83–12.33%), and $MPC_{Sutton\ sulfate} = 4.64\%$ (95% CI: 2.16–6.86%). For diabetes, the corresponding estimates were $MPC_{COH} = 7.50\%$ (95% CI: 1.96–13.34%), $MPC_{Predicted\ PM2.5} = 7.59\%$ (95% CI: 2.36–13.09%), and $MPC_{Sutton\ sulfate} = 4.48\%$ (95% CI: 1.08–7.99%). Among individuals older than 65 years at time of death, we found consistent associations across our metrics of particles for neoplasms and coronary artery diseases. Associations with sulfate mass were also found among elderly persons who died of cardiovascular diseases and of lung cancer. These associations were consistent with linear relationships. The associations found for respiratory diseases and for cardiovascular diseases, especially in the elderly, are in line with some of the current hypotheses regarding mechanisms by which ambient particles may increase daily mortality. The positive associations found for cancer and for diabetes may be understood through a general hypothesis proposed by Frank and Tankersley, who suggested that persons in failing health may be at higher risk for external insults through the failure of regulating physiological set points. The association with diabetes may be interpreted in light of recent toxicological findings that inhalation of urban particles in animals increases blood pressure and plasmatic levels of endothelins that enhance vasoconstriction and alter electrophysiology. Further research to confirm these findings and to determine whether they are causal is warranted. © 2001 Academic Press

Key Words: cause-specific mortality; respiratory diseases; cardiovascular diseases; diabetes mellitus; cancer; ambient air pollution; particulates; total suspended particles; PM_{10}; $PM_{2.5}$; sulfate; coefficient of haze; time series; epidemiology.

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INTRODUCTION

Numerous studies from around the world have shown associations between daily nonaccidental mortality and ambient air particles (Dockery and Pope, 1994; Goldberg, 1996; Schwartz, 1991; Zmirou *et al.*, 1998). These data have been derived mostly from parallel time series studies, in which daily variations in the number of deaths in a population are regressed onto daily fluctuations in ambient concentrations of air pollutants. Studies have been carried out in countries with varied levels of industrialization and air pollution, and the results for nonaccidental deaths have been rather consistent regardless of the extent of pollution or the mix of pollutants (Goldberg, 1996; Schwartz, 1991). A striking aspect of these associations is that levels of the pollutants are within limits set by most national ambient air quality standards.

Despite the consistency of the results, little is known about which specific causes of death contribute to the overall increases in daily mortality. The conventional wisdom is that when daily levels of air pollution become elevated persons with respiratory and cardiovascular diseases are at higher risk of dying, and this conjecture has been confirmed in a number of studies (e.g., Pope *et al.*, 1992; Schwartz and Dockery, 1992; Schwartz, 1993, 1994; Anderson *et al.*, 1996; Bacharova *et al.*, 1996; Ballester *et al.*, 1996, 1997; Ito and Thurston, 1996; Sunyer *et al.*, 1996; Zmirou *et al.*, 1996; Ostro *et al.*, 1996; Dab *et al.*, 1996; Vigotti *et al.*, 1996; Michelozzi *et al.*, 1998). Other causes of death have not been investigated adequately, although there have been two reports of increases in daily mortality from cancer when air pollution is higher (Schwartz and Dockery, 1992; Ito and Thurston, 1996). The investigation of a wider range of causes of death can facilitate the determination of the specific subgroups that are susceptible to the effects of air pollution. In this, the second of a series of papers, we present a time series analysis of cause-specific mortality in Montreal, Quebec; subsequent papers will focus on the identification of subgroups by use of medical information recorded before death.

MATERIALS AND METHODS

We have described in our companion paper (Goldberg *et al.*, 2001) the methodology used in this study (see also Goldberg *et al.*, 2000). In brief, the study population consisted of all residents of Montreal who died in the metropolitan area during the period 1984 to 1993 and who were registered with the universal provincial health insurance plan. Subjects were identified from the computerized provincial database of death certificates that provided identifying information on subjects, date of death, place of death, residence at time of death, and underlying cause of death coded in the Ninth revision of the International Classification of Diseases (ICD9).

During the study period, measurements of particulate air pollution (total suspended particles (TSP), particulates having aerodynamic diameters of 10 and 2.5 μm or under (PM_{10}, $PM_{2.5}$), and sulfates from these metrics) were made at a frequency of every 6 days at several fixed-site monitoring stations in Montreal (Brook *et al.*, 1997a, b). From July 1992 to September 1995, the measurement schedule for PM_{10} and $PM_{2.5}$ was increased at one site to daily sampling (Brook *et al.*, 1997a). Coefficient of haze (COH), which measures organic and inorganic carbon, and criteria gaseous pollutants were measured continuously. We also made use of measurements of daily total sulfate (1986–1993) from an acid rain monitoring station at Sutton, Quebec, a rural community about 150 km southeast from the city. These data represent background levels throughout southwest Quebec, including Montreal (Brook *et al.*, 1997a). The average correlation between sulfate measured at this station and the two Montreal stations was 0.9.

Visibility, barometric pressure, temperature, total precipitation (distinguishing snow from rain), relative humidity, and dew point temperature were measured at Dorval International Airport. Visibility at noon, or at other times of the day when there was no precipitation, was converted into an extinction coefficient (a measure of light scattering and absorption), after accounting for relative humidity (Özkaynak *et al.*, 1985; Kinney and Özkaynak, 1991; Delfino, 1994).

We also developed statistical models for the period 1986–1993 to estimate fine particle mass and sulfate from $PM_{2.5}$ when measurements were not taken, using COH, the extinction coefficient, and sulfate from Sutton as predictor variables (hereafter referred to as predicted $PM_{2.5}$). The R^2 for the prediction model for $PM_{2.5}$ was 0.72 and for sulfate from $PM_{2.5}$ it was 0.80.

We present herein results for selected underlying causes of death that include all of the major diseases (see Table 1). We used quasi-likelihood estimation within the context of the Generalized Additive Models (Hastie and Tibshirani, 1990) to model the expected logarithm of daily counts of cause-specific deaths as functions of the predictor variables. We selected the family of locally weighted regression smoothers (LOESS) for the nonparametric terms. We assumed that the daily counts of death were distributed approximately as a Poisson variate with constant over- or underdispersion and that yearly, seasonal, and subseasonal variations in the mortality time series represented unmeasured processes (e.g., influenza epidemics) that may confound the association between mortality and air pollution. We regressed the natural logarithm of the daily number of deaths on a LOESS term for day-of-study, thus providing an adjustment for seasonal and subseasonal variations (temporal filter), another term to account for annual trends in daily mortality, and LOESS terms to adjust for the potential confounding effects of relevant weather variables. For each underlying cause of death, we used Bartlett's statistic (Priestly, 1981) to select the smoothing bandwidth (span for the LOESS function) of the temporal filter that was consistent with a white noise process. Including this filter and a term for calendar year, we sought the combination of weather variables that yielded a minimum Akaike Information Criterion from among various sets of models that included different weather variables across lags 0 to 5 days.

Single-pollutant models using daily mean values across the fixed-site monitoring stations were considered first. We also estimated mortality with the previous day's level of air pollution (lag 1 day) and with the average of lags 0 to 2 days (referred to as the "3-day mean"). For those pollutants not measured daily, lags were taken by shifting the pollutant time series forward. The 3-day mean could not be calculated for pollutants that were not monitored daily.

Continuous variables representing weather and air pollution were entered into the model nonparametrically using a LOESS smoother that had a span of 50%. Exposure–response functions for the particle variables were plotted from the fitted model, and we used an approximate F test to determine whether the fitted nonparametric smooth was consistent with a linear exposure–response function (Hastie and Tibshirani, 1990).

We also estimated parametric, linear terms for the relative increase in the logarithmic number of daily deaths per unit increase in the pollutant. We calculated the percentage change in the mean number of daily deaths for an increase of the interquartile range (IQ) for each index of particles, i.e., as $[\exp(\beta \times IQ) - 1] \times 100\%$, where β is the estimated regression coefficient. We refer to this quantity as the "mean percentage change" (MPC) in daily mortality. Ninety-five percent confidence intervals (CI) the assumption that the estimated regression coefficient was distributed normally, with the standard error corrected for non-Poisson dispersion.

RESULTS

There were a total of 133,904 nonaccidental deaths during the study period 1984–1993, with neoplasms, cardiovascular diseases, and respiratory diseases accounting for 31.5, 42.8, and 8.5% of all deaths, respectively (Table 1). Some of these cause-specific time series were overdispersed (e.g., cardiovascular diseases), and this arose mostly from strong seasonal fluctuations in mortality. (Graphs of all time series are available from the first author at http://www.epi.mcgill.ca). However, the filtering of each of these time series to white noise (using LOESS with spans of either 91 or 131 days of 3653 days of observations) considerably reduced the overdispersion and the serial autocorrelation.

Mean concentrations of PM_{10} and $PM_{2.5}$ were 32.2 and 17.4 $\mu g/m^3$, respectively, and mean concentrations of ozone and sulfur dioxide were 29.0 and 17.8 $\mu g/m^3$, respectively. (See our companion paper (Goldberg *et al.*, 2001) for details of the distribution of pollutants and weather variables.) Measurements for TSP, PM_{10}, $PM_{2.5}$, and sulfate from these metrics were available for only 12 to 17% of the total number of days on study. Measurements of total sulfate at Sutton were on hand for 8 of the 10 years (1986–1993). Thus, the statistical power for detecting excess daily mortality for these measures of particles was reduced.

Table 2 shows the results of the regression analyses for those underlying causes of death with a mean of more than one death per day. We did not find any consistent positive associations (95% CIs excluding unity) across our indices of particles among persons who died from AIDS and renal diseases (data not shown) or from accidental deaths. Neoplasms, lung cancer, nonmalignant digestive diseases, and neurological conditions were for the most part not found to be associated with particles, except in a few analyses. In addition, all cardiovascular conditions combined and coronary artery diseases were not associated with particle mass, but were rather consistently associated with sulfate particles and the extinction coefficient, particularly at lag 1 day and at the 3-day mean.

The endpoints showing the most consistent positive associations were for deaths from respiratory diseases and from diabetes. However, we did not find statistically significant positive associations for TSP,

TABLE 1

Daily Mortality in Montreal, 1984–1993, by Cause of Death and Age Group

Underlying cause of death	ICD9 codes	Total number of deaths	Number of days in which there were no deaths	Mean	Variance	Variance – mean	Percentiles 25th	50th	75th	100th
Nonaccidental	1-799	133904	0	36.7	51.5	1.40	32	36	41	89
Less than 65 years old		31756	3	8.7	9.1	1.05	7	8	11	22
65 Years old and older		102148	0	28.0	40.2	1.44	24	28	32	79
Neoplasms	140-239	42140	0	11.5	12.0	1.04	9	11	14	25
Less than 65 years old		14023	84	3.8	3.8	1.00	2	4	5	12
65 Years old and older		28117	0	7.7	8.4	1.09	6	8	9	22
Lung cancer	162	11322	174	3.1	3.2	1.03	2	3	4	12
Less than 65 years old		4261	1113	1.2	1.2	1.00	0	1	2	6
65 Years old and older		7061	543	1.9	2.0	1.05	1	2	3	9
Cardiovascular diseases	390-459	57296	0	15.7	19.3	1.23	13	15	18	42
Less than 65 years old		9644	289	2.6	2.8	1.08	1	2	4	11
65 Years old and older		47652	0	13.0	15.7	1.21	10	13	16	40
Coronary artery disease	410-414	34313	0	9.4	10.8	1.15	7	9	12	23
Less than 65 years old		6414	671	1.8	1.8	1.00	1	2	3	8
65 Years old and older		27899	0	7.6	8.5	1.12	5	7	10	19
Respiratory diseases	460-519	11394	216	3.1	3.8	1.23	2	3	4	12
Less than 65 years old		1428	2468	0.4	0.4	1.00	0	0	1	4
65 Years old and older		9966	321	2.7	3.3	1.22	1	2	4	11
Nonmalignant digestive diseases	520-579	5802	740	1.6	1.6	1.00	1	1	2	8
Less than 65 years old		1708	2273	0.5	0.5	1.00	0	0	1	5
65 Years old and older		4094	1195	1.1	1.1	1.00	0	1	2	8
Other nonaccidental causes	580-799	17272	49	4.7	5.7	1.21	3	5	6	16
Less than 65 years old		4953	1025	1.4	1.5	1.07	0	1	2	7
65 Years old and older		12319	156	3.4	3.9	1.15	2	3	5	14
Diabetes	250	3677	1361	1.0	1.1	1.10	0	1	2	7
Less than 65 years old		730	2987	0.2	0.2	1.00	0	0	0	4
65 Years old and older		2947	1655	0.8	0.8	1.00	0	1	1	5
Renal Diseases	580-593	1798	2224	0.5	0.5	1.00	0	0	1	6
Less than 65 years old		233	3425	0.1	0.1	1.00	0	0	0	2
65 Years old and older		1565	2365	0.4	0.4	1.00	0	0	1	6
Neurological conditions	*	4256	1188	1.2	1.3	1.08	0	1	2	7
Less than 65 years old		472	3214	0.1	0.1	1.00	0	0	0	2
65 Years old and older		3784	1361	1.0	1.2	1.20	0	1	2	7
Accidents	800-999	7035	567	1.9	2.1	1.11	1	2	3	9
Less than 65 years old		4603	1083	1.3	1.4	1.08	0	1	2	9
65 Years old and older		2432	1891	0.7	0.7	1.00	0	0	1	7

*013, 036, 046, 290, 294, 310, 320–337, 342, 348, 349, 352, 742

3-day mean were generally stronger than those at lag 0 or lag 1 days. The MPCs in daily mortality from respiratory diseases, evaluated at the 3-day mean for increases across the interquartile ranges, were $MPC_{COH} = 6.90\%$ (95% CI: 3.69–10.21%), $MPC_{Predicted\ PM2.5} = 9.03\%$ (95% CI: 5.83–12.33%), $MPC_{Extinction} = 4.33\%$ (95% CI: 1.49–7.25%), and $MPC_{Sutton\ sulfate} = 4.64\%$ (95% CI: 2.46–6.86%). For diabetes, the corresponding estimates were $MPC_{COH} = 7.50\%$ (95% CI: 1.96–13.34%), $MPC_{Predicted\ PM2.5} = 7.59\%$ (95% CI: 2.36–13.09%), $MPC_{Extinction} = 5.52\%$ (95% CI: 0.60–10.67%), and $MPC_{Sutton\ sulfate} = 4.48\%$ (95% CI: 1.08–7.99%). All of these associations were consistent with a log-linear response function.

Table 3 shows the results for COH, predicted $PM_{2.5}$, and Sutton sulfate after adjusting separately for the effects of SO_2 and O_3 (all pollutants were evaluated at the 3-day mean, and the copollutants were entered into the models using LOESS smooths (spans of 50%)). We found generally that these adjustments increased the standard errors for the metrics of particles and that changes in the estimates could either increase or decrease the estimates of

TABLE 2

Summary Estimates of the Mean Percentage Change in Cause-Specific Daily Mortality across the Interquartile Range of Lagged Exposures to Selected Measures of Particles, Montreal, 1984–1993*

	Lag 0 days		Lag 1 day		3-day mean	
Cause of death	Mean percentage change†	95% CI	Mean percentage change†	95% CI	Mean percentage change†	95% CI
Coefficient of haze (IQ = 1.85 0.1 COH units per 327.8 linear meters)						
Neoplasms	1.15	−0.04-2.35	1.17	0.03-2.39	2.34	0.77-3.93
Lung cancer	2.46	0.19-4.79	0.65	1.61-2.96	3.05	0.04-6.15
Cardiovascular diseases	0.73	−0.30-1.78	0.28	0.75-1.32	0.19	−1.15-1.54
Coronary artery disease	1.28	0.04-2.62	0.46	0.88 1.82	0.94	−0.80-2.72
Respiratory diseases (≥65 years)	4.06	1.59-6.59	4.65	2.24-7.11	6.90	3.69-10.21
Nonmalignant digestive diseases	−1.28	−5.40-3.02	1.90	2.19-6.15	0.67	−2.12-3.54
Accidents	1.05	−1.94 4.12	3.56	0.61-6.59	3.38	−0.45-7.37
Other nonaccidental causes	3.35	1.45-5.28	2.91	1.02-4.83	5.14	2.62-7.71
Neurological conditions	1.98	3.01 7.23	0.66	3.78-5.30	0.12	−2.84-3.17
Diabetes	4.21	0.12-8.47	5.99	1.85-10.30	7.50	1.96-13.34
Total suspended particles (IQ = 28.57 μg/m³)						
Neoplasms	1.53	1.50-4.64	0.26	3.44-3.04		
Lung cancer	6.13	0.19 12.41	6.17	−0.05-12.78		
Cardiovascular diseases	1.86	0.91 4.71	0.26	3.01-2.56		
Coronary artery disease	2.58	1.09 6.38	0.25	3.86-3.50		
Respiratory diseases (≥65 years)	1.83	4.25 8.30	5.59	−0.85-12.45		
Nonmalignant digestive diseases	9.35	1.39 17.94	2.20	6.46 11.65		
Accidents	4.14	11.71 4.08	5.09	12.30-2.70		
Other nonaccidental causes	1.27	3.55 6.32	3.55	−1.65-9.02		
Neurological conditions	2.29	7.32 12.90	12.35	2.00-23.76		
Diabetes	0.99	9.31-12.45	5.92	5.01-18.10		
PM_{10} (IQ 21.32 μg/m³)						
Neoplasms	1.44	1.61 4.58	2.96	6.03 0.21		
Lung cancer	2.34	3.04-8.01	3.01	2.81-9.17		
Cardiovascular diseases	1.54	1.20-4.35	1.92	0.70-4.62		
Coronary artery disease	0.13	3.31-3.69	2.68	0.74-6.23		
Respiratory diseases (≥65 years)	3.16	2.98 9.69	3.05	2.98-9.46		
Nonmalignant digestive diseases	N/C		1.29	6.48-9.70		
Accidents	−6.46	13.34 0.98	3.18	4.17 11.10		
Other nonaccidental causes	0.18	4.85 4.70	4.75	0.27-10.02		
Neurological conditions	N/C		9.75	0.41-19.97		
Diabetes	N/C		13.20	2.69 24.79		
$PM_{2.5}$ (IQ 12.51 μg/m³)						
Neoplasms	1.12	1.50-3.81	0.35	3.07-2.45		
Lung cancer	2.77	−1.90-7.66	3.14	−1.89-8.42		
Cardiovascular diseases	0.69	1.69 3.13	1.68	0.58-3.99		
Coronary artery disease	0.85	2.16 3.96	2.80	0.13-5.82		
Respiratory diseases (≥65 years)	2.11	3.38 7.92	6.35	0.97-12.02		
Nonmalignant digestive diseases	4.50	1.95 11.38	1.18	9.91 4.06		
Accidents	N/C		3.01	3.33-9.76		
Other nonaccidental causes	0.39	4.44 3.83	3.66	0.67-8.18		
Neurological conditions	2.51	10.28 5.94	N/C			
Diabetes	N/C		12.03	3.01 21.84		

TABLE 2—*Continued*

	Lag 0 days		Lag 1 day		3-day mean[c]	
Cause of death	Mean percentage change[b]	95% CI	Mean percentage change[b]	95% CI	Mean percentage change[b]	95% CI
			Predicted PM$_{2.5}$[d] (IQ = 9.50 μg/m^3)			
Neoplasms	1.55	0.29-2.83	1.15	0.11-2.42	1.40	−0.14-2.96
Lung cancer	1.56	−0.82-3.99	0.71	1.70-3.17	1.82	−1.13-4.85
Cardiovascular diseases	0.97	−0.15-2.10	0.77	−0.36-1.91	1.31	−0.06-2.70
Coronary artery disease	1.04	−0.42-2.52	1.17	−0.30-2.67	1.68	−0.12-3.51
Respiratory diseases (≥65 years)	4.24	1.63-6.92	6.01	3.41-8.67	9.03	5.83-12.33
Nonmalignant digestive diseases	4.47	1.08-7.98	0.88	−2.54-4.42	1.90	−2.19-6.15
Accidents	1.08	−2.15-4.41	3.06	−0.08-6.30	2.04	−1.77-6.00
Other nonaccidental causes	3.01	1.05-5.01	2.76	0.78-4.77	3.93	1.51-6.40
Neurological conditions	1.51	−2.15-5.31	−0.03	−3.66-3.73	0.66	−3.78-5.30
Diabetes	5.48	1.24-9.91	5.94	1.69-10.36	7.59	2.36-13.09
			Extinction coefficient (IQ = 0.11 km^{-1})			
Neoplasms	1.16	0.09-2.24	0.81	−0.26-1.89	2.01	0.55-3.50
Lung cancer	1.71	−0.31-3.76	−0.42	−2.50-1.70	2.19	−0.60-5.07
Cardiovascular diseases	0.86	−0.08-1.80	0.60	−0.34-1.54	0.72	−0.55-2.02
Coronary artery disease	1.10	−0.12-2.33	1.25	0.04-2.48	1.89	0.22-3.58
Respiratory diseases (≥65 years)	0.99	−1.09-3.10	2.89	0.87-4.96	4.33	1.49-7.25
Nonmalignant digestive diseases	2.71	−0.07-5.57	1.29	−1.52-4.19	1.81	−2.06-5.84
Accidents	0.07	−2.67-2.87	0.19	−2.90-2.60	−1.37	−5.03-2.44
Other nonaccidental causes	1.42	−0.23-3.09	0.89	−0.80-2.60	2.63	0.35-4.96
Neurological conditions	0.60	−2.62-3.92	−2.04	−5.31-1.35	0.07	−4.29-4.64
Diabetes	4.33	0.83-7.96	2.93	−0.59-6.58	5.52	0.60-10.67
			Sutton sulfate[d] (IQ = 2.50 μg/m^3)			
Neoplasms	0.88	0.07-1.70	0.59	−0.21-1.41	0.75	−0.28-1.78
Lung cancer	0.34	−1.22-1.93	0.60	−0.95-2.19	0.39	−1.60-2.41
Cardiovascular diseases	0.41	0.32-1.14	0.97	0.23-1.72	1.31	0.37-2.26
Coronary artery disease	0.85	−0.12-1.83	1.21	0.25-2.18	1.50	0.28-2.74
Respiratory diseases (≥65 years)	1.28	−0.44-3.02	3.62	1.92-5.34	4.64	2.46-6.86
Nonmalignant digestive diseases	3.00	0.88-5.16	0.63	−2.86-1.66	0.67	−2.12-3.54
Accidents	1.02	−0.93-3.01	1.37	−0.57-3.34	1.73	−0.68-4.20
Other nonaccidental causes	0.69	0.58-1.97	1.16	−0.12-2.45	2.04	0.41-3.69
Neurological conditions	−0.61	−2.95-1.78	0.38	−1.96-2.78	0.12	−2.84-3.17
Diabetes	3.06	0.43-5.76	2.39	−0.25-5.13	4.48	1.08-7.99
			Predicted sulfate from PM$_{2.5}$[d] (IQ = 2.90 μg/m^3)			
Neoplasms	1.27	0.33-2.21	0.82	0.12-1.76	0.97	−0.18-2.15
Lung cancer	0.81	−0.99-2.64	0.76	−1.06-2.61	1.11	−1.13-3.40
Cardiovascular diseases	0.62	−0.23-1.47	0.9[illegible]	0.07-1.79	1.30	0.24-2.37
Coronary artery disease	0.89	0.23-2.02	1.29	0.18-2.42	1.62	0.24-3.02
Respiratory diseases (≥65 years)	2.33	0.37-4.33	4.20	2.24-6.19	6.25	3.80-8.76
Nonmalignant digestive diseases	3.79	1.30-6.33	0.22	−2.34-2.86	1.29	−1.84-4.52
Accidents	1.24	−1.10-3.64	1.90	−0.40-4.26	1.69	−1.13-4.59
Other nonaccidental causes	1.26	−0.20-2.75	1.74	0.25-3.25	2.49	0.66-4.36
Neurological conditions	−0.12	−2.84-2.68	0.01	−2.70-2.80	0.35	3.00-3.81
Diabetes	3.77	0.67-6.95	3.79	0.69-6.98	4.98	1.10-9.00

Note. CI, confidence interval; IQ, interquartile range. See Goldberg *et al.* (2001) for details regarding the distributions of pollutants and weather variables.

[a] The statistical model for each cause of death was E(log(y_i)) = α + loess(i, span = x) + loess year) + multiple weather variables + β · pollutant, where i is an indicator for day and x is the selected span (in days, divided by the total number of days in the study period (3653)).

[b] MPCs calculated for an increase of exposure equal to the interquartile range.

[c] Estimates for the 3-day mean were only calculated particles that were monitored daily

[d] For the period 1986–1993.

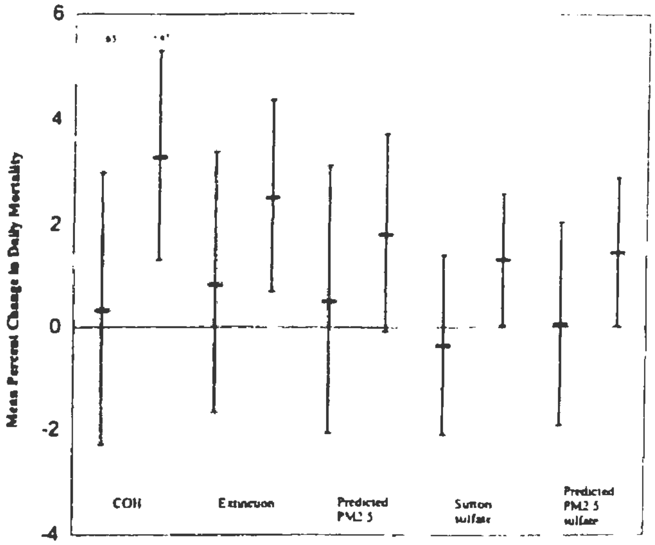

FIG. 1. Mean percentage change in daily mortality from all neoplasms evaluated at the 3-day mean for increases in the interquartile ranges of selected measures of particulates, by age group. The estimated mean percentage change in daily nonaccidental mortality across the interquartile range is shown by the horizontal bars within the vertical lines (95% confidence intervals).

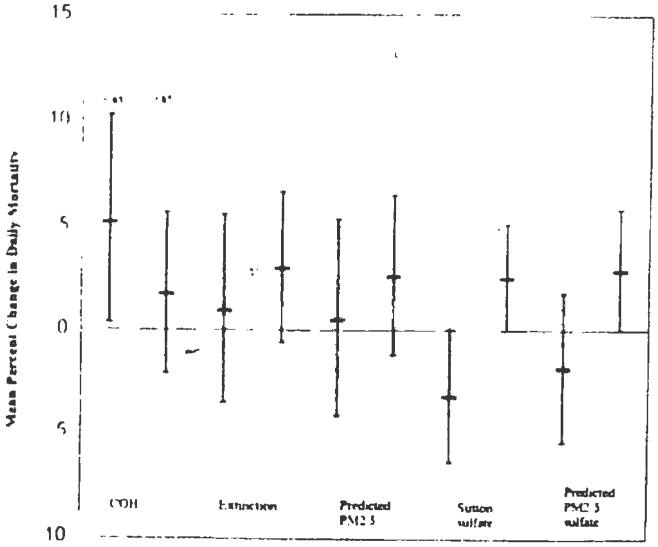

FIG. 2. Mean percentage change in daily mortality from lung cancer evaluated at the 3-day mean for increases in the interquartile ranges of selected measures of particulates, by age group. The estimated mean percentage change in daily nonaccidental mortality across the interquartile range is shown by the horizontal bars within the vertical lines (95% confidence intervals).

effect. Adjustments for SO_2 in the analyses of COH and the extinction coefficient generally attenuated the estimates, and adjustments for O_3 did not greatly alter the estimates. For Sutton sulfate, adjusting for SO_2 did not have a great impact on the estimates but O_3 was found to reduce the estimates, especially for cardiovascular diseases (but not for respiratory diseases or diabetes). We also adjusted for the effects of NO_2 and CO (data not shown); as was the case for SO_2 and O_3, these adjustments either attenuated or did not greatly modify the estimates.

Figures 1–4 show results for selected measures of particles evaluated at the 3-day mean for deaths from cancer, lung cancer, cardiovascular diseases, and coronary artery disease, by age group. We do not show results for diabetes or respiratory diseases as there were too few deaths to conduct reliable age-specific analyses. The figures show rather large confidence intervals that reflect the statistical noise inherent in these time series analyses, particularly for the younger age group. Although we did not find consistent associations for neoplasms in the analyses of both age groups combined, positive associations among the elderly were found across all measures of particles (Fig. 1). For lung cancer and cardiovascular diseases (Figs. 2 and 3, respectively), there was some suggestion of positive effects among the elderly only for sulfate particles. We also found fairly consistent associations among the elderly who died from coronary artery diseases (Fig. 4).

DISCUSSION

We have found positive and statistically significant associations between increases in ambient

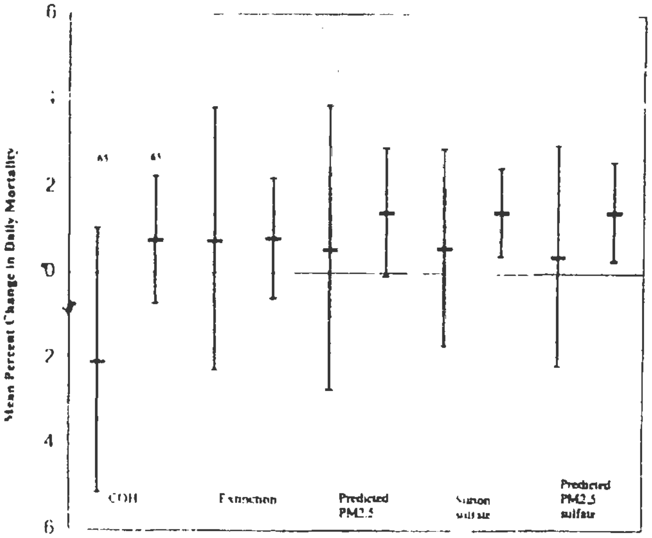

FIG. 3. Mean percentage change in daily mortality from cardiovascular diseases evaluated at the 3-day mean for increases in the interquartile ranges of selected measures of particulates, by age group. The estimated mean percentage change in daily nonaccidental mortality across the interquartile range is shown by the horizontal bars within the vertical lines (95% confidence intervals).

TABLE 3

Estimates of the Mean Percentage Change in Cause-Specific Daily Mortality Adjusted for Sulfur Dioxide or Ozone, across the Interquartile Range for Selected Pollutants Evaluated at the 3-Day Mean, Montreal, 1984–1993[a]

	Cofficient of haze			Predicted $PM_{2.5}$			Extinction coefficient			Sutton sulfate[b]		
Cause of death	Crude	SO_2	O_3	Crude	SO_2	O_3	Crude	SO_2	O_3	Crude	SO_2	O_3
Neoplasms	2.34[c]	0.99	2.39[c]	1.40	0.15	0.75	2.01[c]	1.30	1.65[c]	0.75	0.31	0.22
Lung cancer	3.05[c]	0.42	2.91	1.82	0.40	0.81	2.19	1.00	1.70	0.39	−0.25	−0.79
Cardiovascular diseases	0.19	−1.13	0.39	1.31	1.44	1.15	0.72	0.51	0.51	1.31[c]	1.20[c]	0.81
Coronary artery disease	0.94	−0.92	1.38	1.68	1.76	1.38	1.89[c]	1.40	1.53	1.50[c]	1.34[c]	0.66
Respiratory diseases (≥65 years)	6.90[c]	2.57	5.48[c]	9.03[c]	7.60[c]	6.86[c]	4.33[c]	2.39	2.97[c]	4.64[c]	3.59[c]	3.43[c]
Nonmalignant digestive diseases	0.67	−1.73	−1.28	1.90	1.57	1.23	1.81	2.10	1.42	0.67	0.43	−0.65
Accidents	3.38	6.01[c]	3.59	2.04	3.30	0.94	−1.37	−1.11	−1.71	1.73	2.03	1.20
Other nonaccidental causes	5.14[c]	3.49[c]	4.72[c]	3.93[c]	3.17[c]	2.67[c]	2.63[c]	1.32	1.78	2.04[c]	1.71[c]	1.13
Neurological conditions	0.12	1.13	1.24	0.66	0.40	1.63	0.07	−0.52	−1.12	0.12	−0.23	−2.48
Diabetes	7.50[c]	3.59	9.28[c]	7.59	5.22	7.80[c]	5.52[c]	3.17	5.19[c]	4.48[c]	3.81[c]	4.66[c]

[a] The base statistical model for each cause of death was $E(\log(y_i)) = \alpha + \text{LOESS}(i, \text{span} = x) + \beta_1$ year + multiple weather variables + $\beta_2 \times$ pollutant, where i is an indicator for day and x is the selected span (in days, divided by the total number of days in the study period (3653)). The adjustments for the copollutants included the additional term LOESS(copollutant, span = 0.5). MPCs calculated for an increase of exposure equal to the interquartile range.

[b] For the period 1986–1993.

[c] $t > 1.96$.

particle mass and sulfate mass among persons who died from respiratory diseases and diabetes. Among individuals older than 65 years at time of death, we found consistent associations across our metrics of particles for neoplasms and coronary artery diseases. Associations between sulfate mass were also found among elderly persons who died of cardiovascular diseases and of lung cancer. These associations were consistent with a linear relationship.

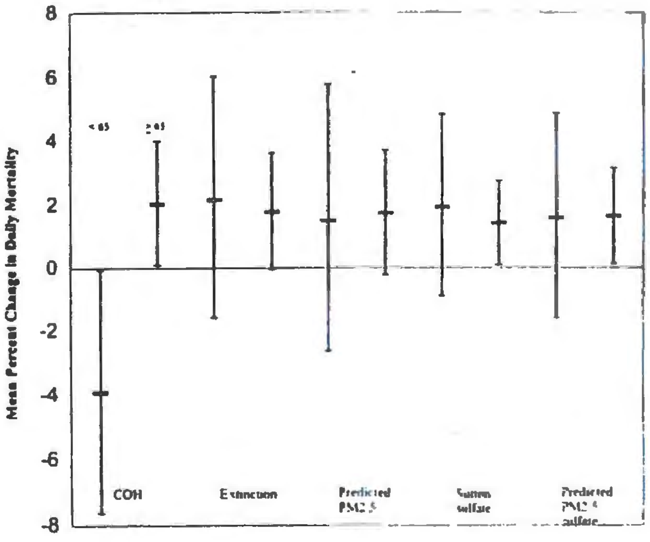

FIG. 4. Mean percentage change in daily mortality from coronary artery diseases evaluated at the 3-day mean for increases in the interquartile ranges of selected measures of particulates, by age group. The estimated mean percentage change in daily nonaccidental mortality across the interquartile range is shown by the horizontal bars within the vertical lines (95% confidence intervals).

We found greater excess mortality for respiratory deaths than for cardiovascular deaths. Scaling our estimates for an increase of 100 μg/m³ in TSP and in PM_{10}, for cardiovascular diseases we found an increase in daily mortality of 6.7 and 7.4%, respectively; for respiratory diseases, the respective estimates were 5.8 and 16.5%. These values are within the ranges that have been reported in the literature (Anderson *et al.*, 1996; Bacharova *et al.*, 1996; Ballester *et al.*, 1996, 1997; Dab *et al.*, 1996; Ito and Thurston, 1996; Michelozzi *et al.*, 1998; Ostro *et al.*, 1996; Pope *et al.*, 1992; Schwartz and Dockery, 1992; Schwartz, 1993, 1994b; Sunyer *et al.*, 1996; Vigotti *et al.*, 1996; Zmirou *et al.*, 1996).

Methodologic Aspects

Data for particle mass were limited by the 6-day measurement schedule; so, we relied on indirect measures. These included the coefficient of haze, which is a reliable measure of the concentration of ambient carbon particles (mostly from internal combustion), the extinction coefficient (which largely measures sulfate), and sulfate from the Sutton acid rain monitoring station. The extinction coefficient is likely to be misclassified more than particle mass mainly because of the subjectivity of the measurements of line-of-sight distance visibility and the approximate formula used to convert to an extinction measure. Measurements of sulfate at the Sutton acid rain station captured regional levels of sulfates but, despite the high correlation with measurements of sulfate in Montreal, was also misclassified because it did not capture local fluctuations. As we did not have a complete series of fine particle measurements, we created one using a linear regression model that included coefficient of haze, sulfate from the Sutton monitoring station, and the extinction coefficient. Although the statistical models provided reasonably good predictions, misclassification of this index should also have reduced power and attenuated estimates of effect.

We assumed that any inaccuracies in the coded underlying causes of death had constant probability distributions over the 10-year period of this study. There are no data reporting the accuracy of underlying causes of death in Quebec. In other jurisdictions, it has been found that the accuracy of coding varies with cause of death (Alderson and Meade, 1967; de Faire *et al.*, 1976; Engel *et al.*, 1980; Percy *et al.*, 1981). Site of cancer is usually coded reasonably accurately (above 80%), but respiratory and cardiovascular diseases are often confused. In particular, when persons have both conditions concurrently and both contributed to death, there may be some uncertainty about which cause should be selected as the primary underlying cause. In other instances, there may be errors in selecting one underlying cause in a complex chain of health events (e.g., cancer leading to pneumonia and then to respiratory failure).

Interpretation

Our results for daily deaths from cardiovascular and respiratory diseases, especially among the elderly, are consistent with other time series studies, recent toxicological studies, and current hypotheses about mechanisms of action. In particular, the positive associations found for elderly persons who died of cardiovascular and respiratory diseases are consonant with the hypothesis of Bates (1992), who suggested that exposure to air pollutants in persons with cardiac disease with myocardial damage may cause acute pulmonary disease, such as bronchiolitis or pneumonia, thereby leading to congestive heart failure. Unfortunately, we were unable to investigate congestive heart failure as there were too few deaths attributed to this cause. Given the high prevalence of congestive heart disease in the elderly, this finding likely reflects the manner in which death certificates are coded. A following paper will deal with this issue more adequately by making use of regularly collected medical data to identify subgroups of the population with these and other diseases. Our findings for an association with acute and chronic coronary artery disease among the elderly is also consistent with the hypothesis of Seaton and collaborators (Seaton *et al.*, 1995), who suggested that in susceptible individuals, exposure to ultrafine particles will invoke alveolar inflammation, release inflammatory mediators, exacerbate lung conditions, and increase coagulability of blood, thereby leading to acute episodes of cardiovascular disease.

The positive associations found for cancer and for diabetes are more difficult to interpret. The former may be understood through a general hypothesis proposed by Frank and Tankersley (1997), who suggested that persons whose health is failing may be at higher risk for external insults, such as exposure to ambient air pollution, through the failure of the regulation of physiological set points. The association with diabetes is unexpected, but is not likely due to misclassification; data from the universal Quebec health insurance plan showed that 84% of persons who had diabetes coded as their underlying cause of death had also been diagnosed with diabetes within 5 years before they died (Goldberg *et al.*, 2001). However, these subjects also had other comorbid diseases, including all other cardiovascular conditions (71%) and chronic lower respiratory diseases (22%).

Recent toxicologic data suggest a mechanism that could link effects in seemingly unrelated diseases such as coronary artery disease, diabetes, and pulmonary diseases. Specifically, it has been shown that inhalation of urban particles in animals not having a structural lung injury increases the circulating levels of endothelins, the most potent vasoconstrictors known (Bouthillier *et al.*, 1998). Elevation of endothelins after inhalation of particles is also associated with a vasopressor response in experimental animals (R. Vincent *et al.*, unpublished). Elevation of circulating endothelin-1 and endothelin-3 has been reported in a number of conditions, including cardiovascular disease, asthma, and diabetes. The peptides have vasoconstrictor and mitogenic effects and may be involved in the pathogenesis of a number of conditions. Diabetes is a condition associated with endothelial dysfunction and often associated with cardiac complications. The toxicologic data suggest that ambient particles and particle-associated chemical species may act principally as endocrine/paracrine modulators; host factors will determine the nature and severity of the health impacts from common pathways of effects in different pathologies. Thus, one may postulate that ambient particles may affect the heart indirectly by a modification of endothelin homeostasis in the lungs. Conceivably, elevated circulating endothelins would impact on cardiac arrhythmia and dysrhythmia, exacerbate congestive heart failure, precipitate an ischemic heart disease, and promote infarct extension, but also possibly affect persons with conditions involving endothelial dysfunction, such as diabetes, atherosclerosis, and kidney diseases.

Further studies are needed to confirm the associations that we have found between these causes of death and daily ambient air particles and to determine whether the associations are a causal result of the particles themselves, a result of a combination with other pollutants, or a result of some other process.

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