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Associations between ambient air pollution and daily mortality among persons with congestive heart failure ☆

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Abstract

We conducted a mortality time series study to investigate the association between daily mortality for congestive heart failure (CHF), and daily concentrations of particles and gaseous pollutants in the ambient air of Montreal, Quebec, during the period 1984–1993. In addition, using data from the universal Quebec Health Insurance Plan, we identified individuals $\geqslant$65 years of age who, one year before death, had a diagnosis of CHF. Fixed-site air pollution monitors in Montreal provided daily mean levels of pollutants. We regressed the logarithm of daily counts of mortality on the daily mean levels of each pollutant, after accounting for seasonal and subseasonal fluctuations in the mortality time series, non-Poisson dispersion, weather variables, and other gaseous and particle pollutants. Using cause of death information, we did not find any associations between daily mortality for CHF and any air pollutants. The analyses of CHF defined from the medical record showed positive associations with coefficient of haze, the extinction coefficient, SO_2, and NO_2. For example, the mean percent increase in daily mortality for an increase in the coefficient of haze across the interquartile range was 4.32% (95% CI: 0.95–7.80%) and for NO_2 it was 4.08% (95% CI: 0.59–7.68%). These effects were generally higher in the warm season.

Keywords: Mortality; Time series; Congestive heart failure; Ambient air pollution; Particulates; Nitrogen dioxide

1. Introduction

There is substantial and consistent evidence for an association between increases in levels of ambient air pollution and daily mortality (Dockery and Schwartz, 1995; Goldberg, 1996; Pope III, et al., 1995; Schwartz, 1992; Schwartz, 1994). It has been suggested that only persons in poor health are at high risk (Bates, 1992; Frank and Tankersley, 2002; Goldberg, 1996). A principal hypothesis is that exposure to air pollutants may cause acute pulmonary disease, such as bronchiolitis or pneumonia, thereby leading to congestive heart failure (CHF) in persons with myocardial damage or cardiac disease (Bates, 1992). Alternatively, exposure to ultrafine particles may invoke alveolar inflammation, release inflammatory mediators, exacerbate lung conditions, and increase coagulability of blood thereby leading to acute episodes of cardiovascular disease (Seaton et al., 1995). By extension, it can be hypothesized that persons with CHF may be particularly susceptible to the effects of air pollution (Bates, 1992; Kodavanti et al., 1998; Seaton et al., 1995). In the few

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studies in which CHF has been investigated, it was found generally that daily hospitalizations for CHF (Burnett et al., 1997; Morris et al., 1995; Morris and Naumova, 1998; Poloniecki et al., 1997; Schwartz, 1997) and daily mortality among persons with CHF (Kwon et al., 2001) increased when levels of ambient particles and gaseous pollutants increased. In the present paper, we present a time series investigation to determine whether persons with preexisting CHF are at higher risk of dying when levels of ambient air pollution increase.

2. Materials and methods

2.1. The study population

The study took place in Montreal, Quebec, a large metropolitan area that experiences relatively low levels of air pollution (Goldberg et al., 2000; 2001a, b). Subjects were residents of Montreal who died in the metropolitan area during the period 1984–1993 and who were registered with the universal Quebec Health Insurance Plan (QHIP). They were first identified from the computerized provincial database of death certificates and each deceased subject was then linked to the population register of the QHIP.

2.2. Definitions of CHF

We conducted separate analyses for subjects (1) who had an underlying cause of death of CHF (International Classification of Diseases, Ninth Revision (ICD9), 428 (World Health Organization, 1980)) or (2) who were attributed as having CHF before dying from a natural cause (independent of the cause provided on the death certificate). For the latter, we made use of diagnoses and specific health services rendered by physicians both in and out of hospital as well as filled prescriptions reimbursed by the QHIP. The QHIP provides universal coverage for all costs of medical services dispensed in-province and it provides complete or partial coverage for services and hospital admissions out-of-province. Individuals are given unique health insurance plan numbers and these are recorded on each medical transaction and are used administratively to check the validity of claims. Physicians are paid by the QHIP on a fee-for-service basis and out-of-province health care is paid by the patient and reimbursed partially or in full by the QHIP. This leads to almost complete reporting to the QHIP. Laboratory tests and the results from these tests are not part of the database. When submitting each bill for service, the physician had the option to record one ICD9 diagnostic code. Unlike the billing data, which are examined by the QHIP for consistency and accuracy, diagnoses were not verified. In addition, most physicians used a restricted set of ICD9 codes reflecting the mix of patients that consulted them. As well, the QHIP paid the costs of prescriptions for persons aged 65 and over. The information on dispensed prescriptions included the date, the name and generic type of medication, quantity, duration of prescription, and authorization for refills.

We classified a subject as having CHF before death if (Goldberg et al., 2000): (1) for ages under 65 years, there were at least two recorded billings with a diagnosis of ICD9 428 and (2) for ages 65 years and over, there were at least two recorded billings with a diagnosis of ICD9 428 or one billing with ICD9 428 and at least one prescription for diuretics. We used a 1-year time window for these events to account for broad variations in the frequency of physician visits, missing diagnostic information on the billing record (about one-half of the billing records have diagnoses listed), and variations in how pharmaceuticals are prescribed by physicians.

2.3. Air pollution and weather data

Measurements of sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and carbon monoxide (CO) were made every 2 h at fixed-site monitoring stations in Montreal. SO_2 was measured at 13 stations using ultraviolet fluorescence and electrical conductivity from changes in chemical composition of a bromine solution (Philips 9700 and Monitor Lab 8850); NO_2 was measured at eight stations using chemiluminescence (Thermo Electron 14B); and CO was measured at 12 stations using infrared absorption (Thermo Electron 48). The coefficient of haze (COH), which measures organic and inorganic carbon, was also measured every 2 h at several fixed-site monitoring stations in Montreal. Particle mass (total suspended particles (TSP)), particles having aerodynamic diameters of 10 μm and under and 2.5 μm and under (PM_{10}, $PM_{2.5}$, respectively), and sulfate from these metrics) was measured at a frequency of every 6 days (Brook et al., 1997a, b). From July 1992 to September 1995, the measurement schedule for PM_{10} and $PM_{2.5}$ increased at one site to daily sampling. We also made use of measurements of daily total sulfates (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., 1997b). The average correlation between sulfates 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 was converted into an extinction coefficient (a measure of light scattering and absorption, due mostly to sulfates) after accounting for relative humidity (Delfino et al., 1994;

Kinney and Ozkaynak, 1991; Ozkaynak et al., 1985). We used the measurement at noon when there was no precipitation or the hour closest to noon without precipitation.

We also developed statistical models to estimate fine particle mass and sulfates from $PM_{2.5}$ (hereafter referred to as predicted $PM_{2.5}$) when measurements during 1986–1993 were not taken (Goldberg et al., 2000; 2001a, b). COH, the extinction coefficient, and total sulfates from Sutton were used as predictor variables, and the R^2 for the prediction model was 0.72 for $PM_{2.5}$ and for sulfate from $PM_{2.5}$ it was 0.80.

2.4. Statistical methods

For the two definitions of CHF, separate analyses were conducted to estimate associations with daily levels of air pollution and day of death. In both sets of analyses, we excluded subjects whose deaths were from accidents, poisonings, and injuries (ICD9 $\geqslant$800). We ignored the underlying cause of death in the analyses that made use of QHIP data to identify persons with CHF before death. Average daily concentrations of pollutants were used in all analyses, and these were derived by taking a simple daily average for each monitor and then averaging these to obtain a final daily mean value. We assumed that the daily counts of death were distributed approximately as a Poisson variate with constant over- or under-dispersion and we used quasi-likelihood estimation to model the logarithm of daily counts of cause-specific deaths as functions of the predictor variables. Numerical problems (Dominici et al., 2002; Ramsay et al., 2002) have been found recently with the use of regression splines or locally weighted regression smoothers within the generalized additive models framework (Hastie and Tibshirani, 1990) to estimate non-parametric smoothings for continuous covariates. Instead, we used natural splines to model the effects of continuous covariates. Thus, within the context of a generalized linear Poisson model, we regressed the natural logarithm of the daily number of deaths on the natural spline for day-of-study, thus providing an adjustment for seasonal and subseasonal variations (temporal filter), on a dummy variable to account for annual trends in daily mortality, and on natural splines of potential confounding effects of relevant weather variables. For each analysis, we selected the temporal filter having the number of knots that produced a filtered time series that was consistent with a white noise process, using Bartlett's statistic (Priestly, 1981). This produced a residual time series that had the least amount of serial autocorrelation. We then sought the combination of weather variables that yielded a minimum value of the Aikake Information Criterion (Hastie and Tibshirani, 1990) (a penalized measure of the deviance) from among various sets of models that included different weather variables across lags 0–5 days.

Filtered and weather-adjusted single-pollutant models using daily mean values for the concurrent day across the fixed-site monitoring stations were considered. We also estimated mortality with the previous day's level of air pollution (lag 1 day) as well as with the average of lags of 0–2 days (referred to as the "3-day mean"). These lag periods were selected a priori in order to investigate the short-term effects of pollution on mortality. Because pollutants can vary considerably by season, especially ozone and particles, we also assessed associations according to a "cold season" (October–March) and a "warm season" (April–September). Last, we were interested in determining whether effects of pollution may affect women and men differently and, thus, separate analyses were conducted according to sex.

Assuming linearity in the response function for the air pollution variables, we estimated the relative increase in the logarithmic number of daily deaths per unit increase in the concentration of the various pollutants. The percent change in the mean number of daily deaths for an increase of pollutant equal to its interquartile range was calculated (referred to as the mean percent change in daily mortality (MPC)). Associated upper and lower 95% confidence limits (95% CI) on the mean percent change were obtained assuming that the estimated regression coefficient was distributed normally, with the standard error corrected for non-Poisson dispersion.

3. Results

There were a total of 133,904 non-accidental deaths during the study period 1984–1993. CHF accounted for 2.1% of these (2,740 deaths; Table 1), with the majority among persons age 65 years and over. All results presented subsequently are for this age group only. Using our definition of CHF from the morbidity data, we found 14,615 subjects 65 years of age and over who had CHF before death (Table 1). Of these subjects, 66% were coded as having a circulatory underlying cause of death, and only 6.3% were attributed as dying from CHF. Among those subjects whose underlying cause of death was given as CHF, only 37% were classified from the QHIP data as having CHF before death.

Figs. 1 and 2 and Table 1 show that there was little overdispersion in either of the CHF mortality time series. Table 1 also shows the distributions of pollutants and weather variables; levels of pollutants in Montreal are fairly low with respect to other North American and European cities.

For the analyses of CHF defined using the underlying cause of death, we used a natural spline having 71 degrees of freedom to adjust for temporal trends and we

Table 1
Distribution of essential variables, Montreal, 1984–1993

	Units	Number of days of measurements	Mean	Standard deviation	Minimum	Percentiles				Inter-quartile range
						25th	50th	75th	100th	
Congestive heart failure										
Coded as underlying cause of death										
⩾65 years	2528	1795	0.7	0.85	0	0	0	1	7	1.0
Total	2740	1884	0.75	0.89	0	0	1	1	7	1.0
Morbidity 1 year before death										
⩾65 years	14615	3552	4.0	2.19	0	2	4	5	15	3.0
Total	16794	2592	4.6	2.35	0	3	4	6	16	3.0
TSP	$\mu g/m^3$	603	53.1	22.6	14.6	37.0	48.7	65.6	211.1	28.57
PM_{10}	$\mu g/m^3$	624	32.2	17.6	6.5	19.7	28.5	41.1	120.5	21.32
$PM_{2.5}$	$\mu g/m^3$	636	17.4	11.4	2.2	9.4	14.7	21.9	72.0	12.51
Sulfate from PM_{10}	$\mu g/m^3$	437	4.7	4.4	0.3	1.9	3.6	5.7	30.7	3.84
Sulfate from $PM_{2.5}$	$\mu g/m^3$	446	4.3	4.2	0.2	1.6	3.1	5.1	29.2	3.51
Sulfate from TSP	$\mu g/m^3$	607	4.3	2.9	0.3	2.3	3.6	5.3	19.2	3.02
Sulfate from the Sutton monitorino Station[a]	$\mu g/m^3$	2680	3.3	3.6	0	1.3	2.2	3.8	30.0	2.50
COH	0.1 COH Units per 327.8 linear meters	3653	2.4	1.5	0.1	1.3	2.1	3.2	15.6	1.85
Predicted $PM_{2.5}$[a]	$\mu g/m^3$	3653	17.6	8.8	4.6	11.5	15.4	21.0	71.7	9.5
Predicted Sulfate from PM_2[a]	$\mu g/m^3$	3653	4.1	3.6	0.02	1.9	3.1	4.8	30.1	2.9
Extinction	km^{-1}	3454	0.15	0.10	0.01	0.06	0.15	0.17	1.87	0.11
SO_2	$\mu g/m^3$	3653	17.8	11.2	3.9	10.3	14.6	21.8	105.7	11.50
NO_2	$\mu g/m^3$	3653	41.7	15.4	8.8	30.9	39.5	50.2	143.5	19.34
CO	ppm	3653	0.8	0.5	0.1	0.5	0.7	1.0	5.1	0.50
O_3	$\mu g/m^3$	3653	29.0	17.1	2.8	16.6	26.0	37.9	163.9	21.34
Mean temperature	°C	3653	6.4	11.8	−27.3	−2.6	7.5	16.5	28.8	19.10
Change in maximum temperature from previous day	°C	3653	0.0	4.7	−25.0	−2.5	0.4	2.8	19.4	5.30
Mean dew point temperature	°C	3653	1.2	11.6	−33.8	−6.6	2.0	10.8	23.1	17.40
Relative humidity	%	3653	69.4	11.9	33.0	61.0	70.0	78.0	99.0	17.00
Change in barometric pressure from previous day	kPa	3653	0.0	0.9	−4.2	−0.5	0.0	0.6	4.4	1.10

[a] For the period 1986–1993.

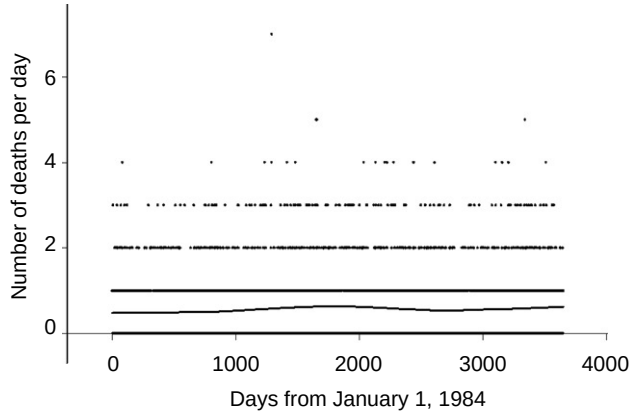

Fig. 1. Scatterplot of daily number of nonaccidental deaths among persons age 65 years and over who were classified as dying from CHF. The solid line is the locally weighted regression smoother (LOESS) smooth representing the long-term trend in the data (span of 50% of the data). The total number of days in the time series is 3653.

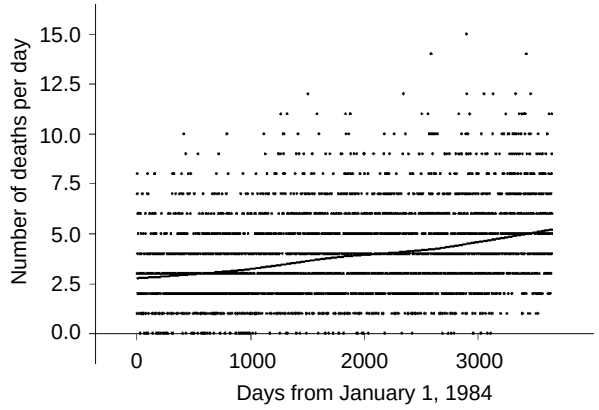

Fig. 2. Scatterplot of daily number of non-accidental deaths among persons age 65 years and over who were classified as having CHF before death. The solid line is the LOESS smooth representing the long-term trend in the data (span of 50% of the data). The total number of days in the time series is 3653.

found that a natural spline on four degrees of freedom for mean temperature and a linear term for change in barometric pressure from the previous day, both evaluated at lag 0 days, minimized the AIC. We did not find any statistically significant associations for any of the pollutants evaluated at any of the three lag periods considered (Table 2).

Among persons classified as having CHF 1 year before death using the QHIP data, we used a natural spline having 61 degrees of freedom to adjust for temporal trends and we found that a natural spline on 3 degrees of freedom for mean temperature and a natural spline on two degrees of freedom for change in barometric pressure from the previous day, both evaluated at lag 0 days, minimized the AIC. Daily mortality was significantly increased at all three lag periods for COH and for sulfur dioxide (Table 3). We also found that nitrogen dioxide was associated positively with CHF at lag 1 day and at the 3-day mean. At the 3-day mean, the MPCs across all pollutants varied between 0.56% and 4.67%.

Figs. 3 and 4 show the results of the analyses for the 3-day mean, adjusted simultaneously for other pollutants (CO, NO_2, SO_2, ozone, and the COH (a marker for particle pollution)). For mortality from CHF (Fig. 3), the adjustments did not alter the findings that were reported in Table 3. For pre-existing CHF derived from the QHIP data (Fig. 4), except for ozone, all of these adjustments attenuated the MPCs and generally increased the confidence intervals.

Fig. 5 shows separate analyses of preexisting CHF for the cold and warm seasons. The effects were higher in the warm season for all pollutants except the two measures of sulfates, and COH and SO_2 also displayed significant positive effects in the cold season. Fig. 6

Table 2
Summary estimates of the mean percent change in daily mortality from CHF among persons 65 years of age and over across the interquartile range of mean daily concentrations of selected particulate and gaseous pollutants, Montreal, 1984–1993[a]

Pollutant	Lag 0 days		Lag 1 day		Three-day mean	
	Mean percent change[b]	95% CI	Mean percent change[b]	95% CI	Mean percent change[b]	95% CI
COH	−0.03	−5.20 to 5.43	−1.06	−6.37 to 4.56	−1.93	−9.22 to 5.94
Extinction	0.76	−3.78 to 5.51	−1.87	−6.62 to 3.13	−1.14	−7.82 to 6.02
Predicted $PM_{2.5}$[b]	1.54	−3.90 to 7.29	−0.76	−6.84 to 5.71	2.00	−5.58 to 10.18
Sulfate from the Sutton monitoring station[b]	0.29	−3.18 to 3.88	−0.08	−4.09 to 4.10	1.73	−3.48 to 7.23
Predicted Sulfate from $PM_{2.5}$[b]	0.87	−3.22 to 5.13	−1.01	−5.72 to 3.93	2.08	−3.84 to 8.37
SO_2	0.92	−4.84 to 7.04	−0.05	−5.62 to 5.86	0.05	−7.45 to 8.16
NO_2	1.04	−4.55 to 6.96	0.94	−4.96 to 7.20	0.10	−7.58 to 8.43
CO	−0.99	−6.31 to 4.63	0.12	−5.29 to 5.84	−1.38	−8.81 to 6.66
O_3	−0.21	−6.66 to 6.69	5.27	−2.49 to 13.64	4.54	−5.64 to 15.81

[a] Adjusted for temporal effects, calendar year, mean temperature, change in barometric pressure from the previous 24 h, and an interaction term between temperature and barometric pressure.
[b] For the period 1986–1993.

Table 3
Summary estimates of the mean percent change in daily mortality among persons classified as having CHF before death, 65 years of age and over, across the interquartile range of mean daily concentrations of selected participate and 'gaseous pollutants, Montreal, 1984–1993[a]

Pollutant	Lag 0 days		Lag 1 day		Three-day mean	
	Mean percent change[b]	95% CI	Mean percent change[b]	95% CI	Mean percent change[b]	95% CI
COH	2.78	0.48 to 5.13	3.72	1.36 to 6.14	4.32	0.95 to 7.80
Extinction	2.36	0.42 to 4.34	1.20	−0.69 to 3.13	2.08	−0.67 to 4.92
Predicted $PM_{2.5}$[b]	2.53	−0.04 to 5.18	1.69	−0.79 to 4.23	2.15	−1.03 to 5.43
Sulfate from the Sutton monitoring station[b]	0.66	−1.03 to 2.39	0.47	−1.08 to 2.04	0.56	−1.53 to 2.69
Predicted Sulfate from $PM_{2.5}$[b]	1.61	−0.39 to 3.64	0.68	−1.14 to 2.54	1.15	−1.23 to 3.58
SO_2	3.30	0.86 to 5.79	3.28	0.83 to 5.80	4.67	1.30 to 8.14
NO_2	2.37	−0.11 to 4.92	3.25	0.66 to 5.91	4.08	0.59 to 7.68
CO	2.10	−0.24 to 4.49	2.28	−0.09 to 4.72	2.86	−0.46 to 6.29
O_3	2.13	−1.14 to 5.50	−0.08	−2.93 to 2.85	2.34	−1.78 to 6.63

[a] Adjusted for temporal effects, calendar year, mean temperature, change in barometric pressure from the previous 24 h, and an interaction term between temperature and barometric pressure.
[b] For the period 1986–1993.

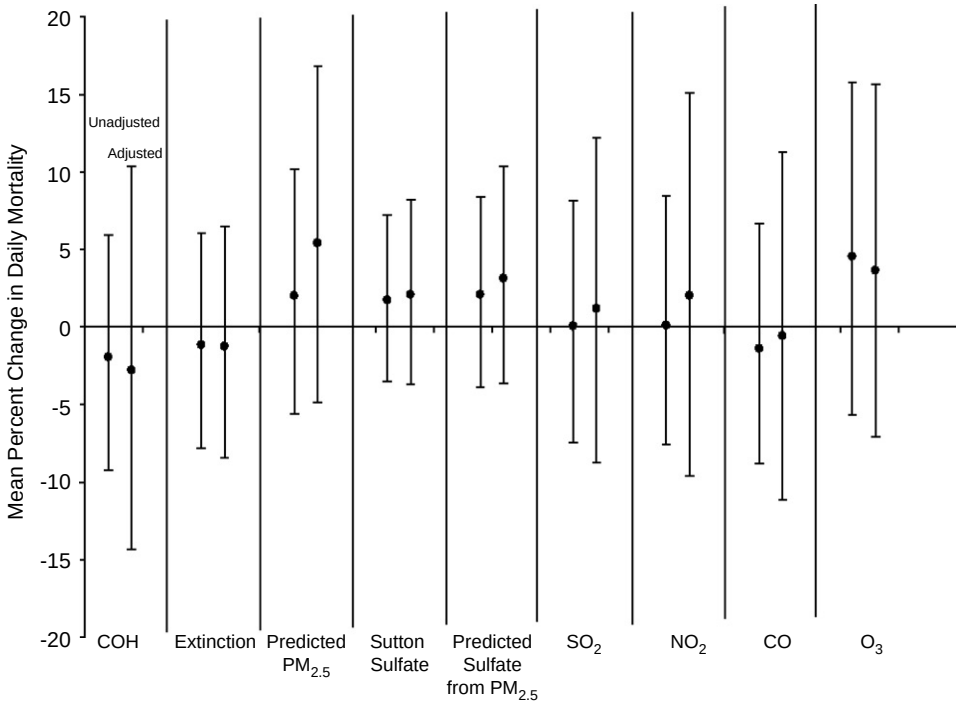

Fig. 3. Mean percent change in daily mortality among subjects age 65 years and over who died from CHF for increases of the interquartile range of selected pollutants, adjusted for the variables listed in footnote (a) of Table 2 and other pollutants. All pollutants were evaluated at the 3-day mean. The estimated mean percent change in daily cause-specific mortality across the interquartile range is shown by the horizontal bars within the vertical lines (95% confidence intervals). The statistical adjustments for the particle metrics included terms for the other gaseous pollutants (CO, SO_2, NO_2, O_3); these gaseous pollutants were adjusted for each other and for the COH.

shows the analyses for CHF morbidity stratified by sex. For all pollutants but ozone, larger effects were found in men than in women, although the differences were not significant statistically.

4. Discussion

Among those persons whose underlying cause of death was CHF, we found no statistically significant

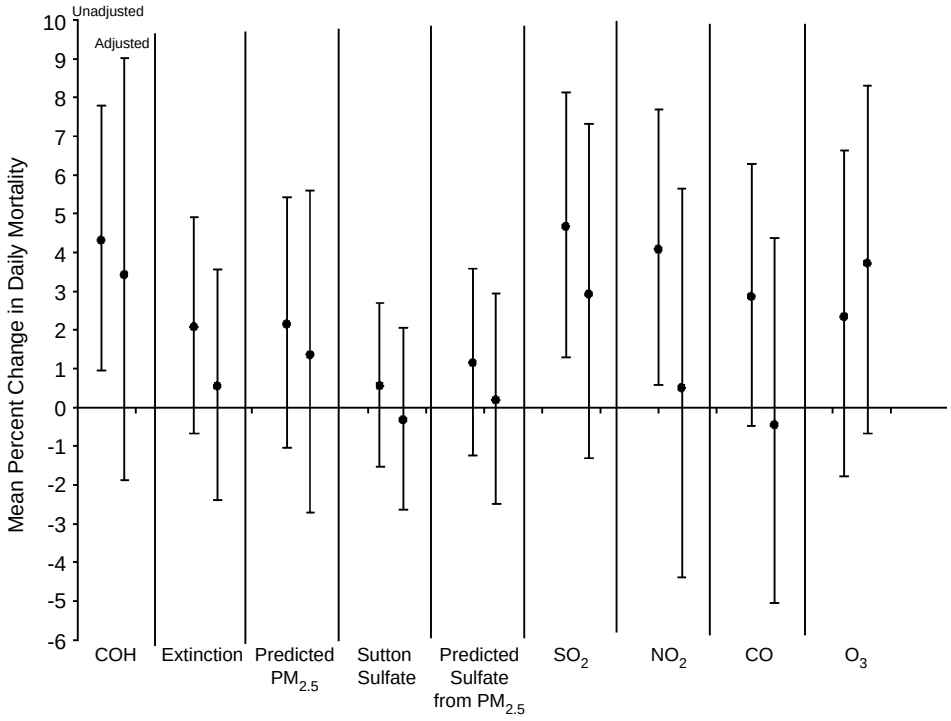

Fig. 4. Mean percent change in daily mortality among subjects 65 years and over who were classified as having CHF before death, adjusted for the variables listed in footnote (a) of Table 2 and for other pollutants. All pollutants were evaluated at the 3-day mean. The estimated mean percent change in daily cause-specific mortality across the interquartile range is shown by the horizontal bars within the vertical lines (95% confidence intervals). The statistical adjustments for the particle metrics included terms for the other gaseous pollutants (CO, SO_2, NO_2, O_3); these gaseous pollutants were adjusted for each other and for the COH.

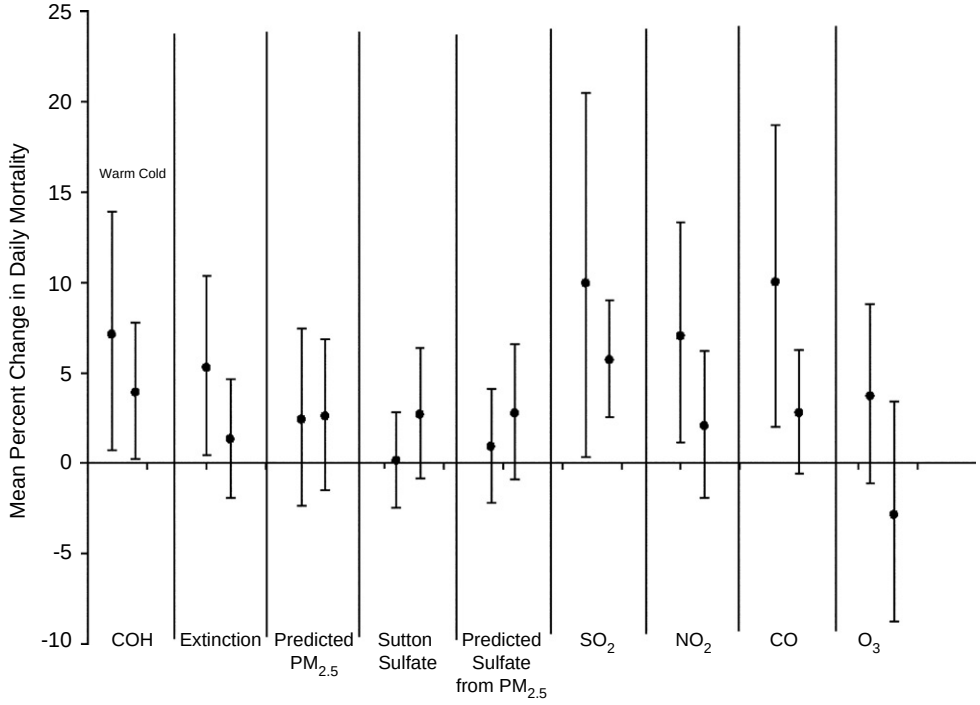

Fig. 5. Mean percent change in daily mortality among subjects 65 years and over who were classified as having CHF before death, according to season, adjusted for the variables listed in footnote (a) of Table 2. The "warm season" includes the months April–September. All pollutants were evaluated at the 3-day mean. The estimated mean percent change in daily cause-specific mortality across the interquartile range is shown by the horizontal bars within the vertical lines (95%, confidence intervals).

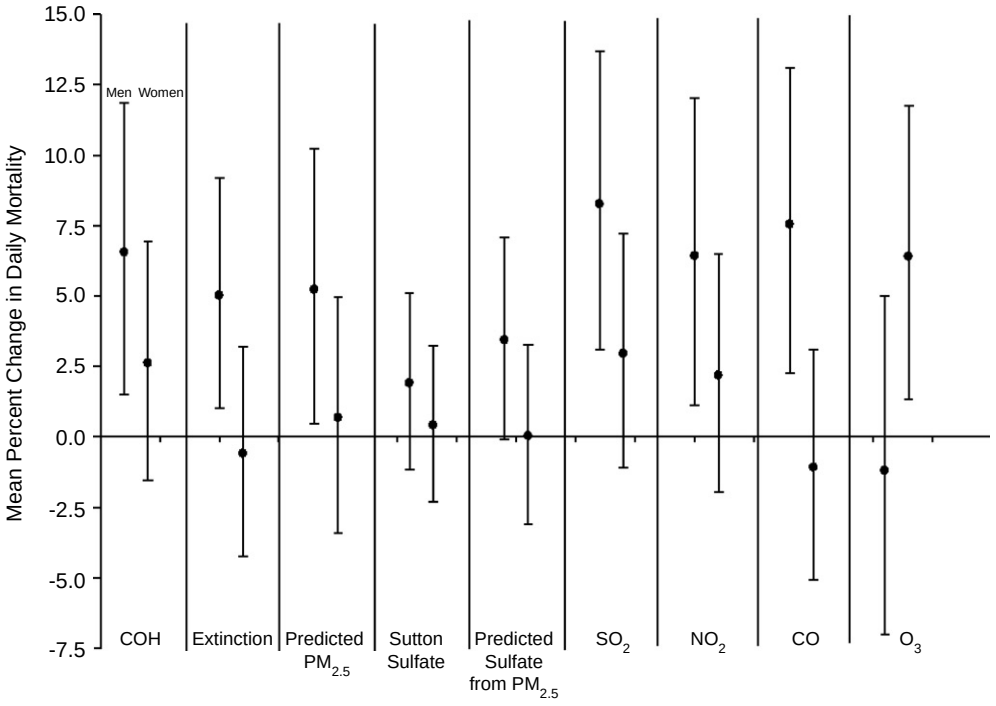

Fig. 6. Mean percent change in daily mortality among subjects 65 years and over classified as having CHF before death, according to gender, adjusted for the variables listed in footnote (a) of Table 2. All Pollutants were evaluated at the three-day mean. The estimated mean percent change in daily cause-specific mortality across the interquartile range is shown by the horizontal bars within the vertical lines (95% confidence intervals).

associations with any of the pollutants. Among persons who were classified as having CHF within 1 year of death, we found that daily mortality increased in a linear fashion for COH, the extinction coefficient, SO_2, and NO_2, and that these associations were more pronounced in the warm season. We did not find any associations with specific measures of fine particles or sulfates.

There are no data reporting the accuracy of underlying causes of death in Quebec, but 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. Given these facts, it is therefore not surprising that we found few individuals who were diagnosed with CHF, and our negative findings are likely a result of limited statistical power and misclassification.

There are a few time series studies of hospitalization for CHF (Burnett et al., 1997; Morris et al., 1995; Morris and Naumova, 1998; Poloniecki et al., 1997; Schwartz and Morris, 1995) and mortality from CHF (Kwon et al., 2001) (Table 4). Associations between daily hospitalizations for CHF and most pollutants (CO, NO_2, SO_2, ozone, PM_{10}) were found in three American studies (Morris et al., 1995; Morris and Naumova, 1998; Schwartz and Morris, 1995). Another study of hospital admissions (Burnett et al., 1997) in the 10 largest cities in Canada revealed positive associations with CO, NO_2, SO_2, and COH. In one study, an interaction between temperature and CO was found (Morris and Naumova, 1998). No associations were found between daily hospitalization and air pollution in one study conducted in London, England (Cendon et al., 1997). On the other hand, in a follow-up of a cohort of persons hospitalized for CHF, Kwon et al. (2001) found results similar to ours and, in particular, observed stronger associations with daily mortality in the CHF cohort than among the general population.

Our findings need to be interpreted in light of the assumptions, strengths, and limitations of the study design. There tends to be a high degree of correlation among day-to-day changes in the concentrations of air pollutants (gases and particles) in urban air. This is due to similarities in the sources, atmospheric chemical processes, and influences of weather among urban pollutants. These considerations suggest that adjusting one pollutant for another may not be warranted. In addition, in a recent personal monitoring study, Sarnat and collaborators (2001) concluded that such adjustments for $PM_{2.5}$, in particular, are not justified because

Table 4
Summary of evidence of associations between hospitalization or mortality and increases in ambient air pollution

Reference and publication year	Place, dates, population	Outcome measure	Mean number of events per day	Pollutant	Meaner median concentration	Increase in levels of pollutants used to calculate relative increases in daily number of events (assumes a linear response function)	Relative increase in daily number of events per metric	95% Confidence interval or t-ratio
Schwartz and Morris (1995)	Detroit, 1986–1989, ⩾65 years	Hospital admissions for heart failure (ICD 9428)	26.6	PM_{10}	48.0	Per IQR: 32[μg/m^J mean of pollutant at lags 0 and 1 days	1.032	1.012–1.052
				Ozone	41.0	Per IQR: 28 ppb, no lag	1.022	0.997–1.048
				SO_2	25.4	Per IQR: 18 ppb, no lag	1.002	0.978–1.017
				CO	2.38	Per IQR: 1.28 ppm, no lag	1.022	1.011–1.033
Morris et al. (1995)	Chicago	Primary hospital admissions for heart failure (ICD9 428)	33.7	CO	1.8–5.6	Per 10 ppm	1.22[a]	1.14–1.31
	Detroit		16.3	NO_2	0.04–0.08	Per 0.1 ppm	1.10[a]	1.06–1.15
	Houston		9.3	SO_2	0.10–0.32	Per 0.05 ppm	1.05[a]	0.99–1.11
	Los Angeles		39.5	Ozone	0.039–t.075 (range of means across cities)	Per 0.12 ppm	1.00[a]	0.95–1.06
	Milwaukee		7.4					
	New York		33.0					
	Philadelphia 1986–1989, ⩾65 years		17.0					
Poloniecki et al. (1997)	London, 1987–1994	Hospital admissions for heart failure (ICD9 428)	24.6	Ozone	13	Per 1 ppb lagged 1 day	0.99	0.96–1.03
				NO_2	35	Per 1 ppb lagged 1 day	1.00	0.98–1.02
				SO_2	6	Per 1 ppb lagged 1 day	1.01	0.99–1.03
				CO	0.9	Per 1 ppm lagged 1 day	1.01	0.99–1.03
				Black smoke	12	Per 1 μg/m^3 lagged 1 day	1.01	0.99–11.03

Burnett et al. (1997)	10 Canadian cities[b], 1981–1991, ⩾65 years	Hospital admissions for congestive heart failure (ICD9428)	39	CO	1.59	Per 8-h average ppm; no lag	1.04	5.1
				NO_2	23	Per 23 ppb; no lag	1.04	3.0
				COH	0.3	Per 0.3×10^3 linear feet; no lag	1.00	3.6
				SO_2	4.7	Per 4.7 ppb; no lag	1.02	2.4
				Ozone	16	Per 16 ppb; no lag	0.97	1.6
Morris and Naumova (1998)	Chicago, 1986–1989, ⩾65 years	Primary hospital admissions for heart failure (ICD9428)	34	CO	2.51	Per 3.054 ppm 75^{th} percentile	1.09	1.06–1.12
				NO_2	0.044	Per 0.053 ppm 75^{th} percentile	1.04	1.01–1.06
				SO_2	0.025	Per 0.030 ppm 75^{th} percentile	1.09	1.05–1.13
				Ozone	0.039	Per 0.051 ppm 75^{th} percentile	1.03	0.99–1.07
				PM_{10}	41.0	Per 51.0 ppm 75^{th} percentile	1.04	1.01–1.07
Kwon et al. (2001)	Seoul, Korea, all ages, cohort of persons with a primary hospital admission for heart failure (ICD9 428), 1994–996	Daily mortality from 1994–1998 of cohort	1,807 deaths total	CO	0.11 ppm	Per 0.59 ppm (IQR)	1.054	0.991–1.121
				NO_2	30.6 ppb	Per 14.6 ppb (IQR)	1.065	0.995–1.139
				SO_2	10.8 ppb	Per 9.9 ppb (IQR)	1.070	0.997–1.147
				Ozone	28.2 ppb	Per 20.5 ppb (IQR)	1.034	0.966–1.108
				PM_{10}	63.7 μg/m^3	Per 42.1 μg/m^3 (IQR)	1.058	0.989–1.131

Note: Lag x refers to evaluating the association using values of exposure x days before the event. PM_{10}, particles having an aerodynamic diameter of 10 μm; COH, coefficient of haze (a measure of ambient carbon); CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; ppm(b), parts per million (billion); IQR, interquartile range.

[a] Estimated from a weighted meta-regression analysis across the estimates in each of the seven cities.

[b] Montreal, Ottawa, Toronto, Hamilton, London, Windsor, Winnipeg, Edmonton, Calgary.

of the lack of correlations between ambient and 24-h integrated personal exposures to air pollutants. However, this conclusion may not apply to time series studies in which the exposure metrics are concentrations of ambient air pollutants. We thus believe that the multipollutant analyses that accounted for the joint effects of NO_2, SO_2, CO_3 and ambient particles needs to be interpreted cautiously, as these adjustments may not, in fact, represent unbiased estimates of effect if these pollutants are not true confounding variables. Thus, these multipollutant models should be considered as sensitivity analyses that may represent a plausible range of health effects.

We could not control for the effects of infectious disease epidemics (e.g., influenza, which occurs mostly in the fall and winter when particle levels are increased) because there are no databases that could be used for this purpose. These epidemics occur mostly in the winter months and the effects of ozone is mostly in the warm months of the year, so that these epidemics should not have confounded the warm-season-specific estimates. As well, the temporal filter should have adjusted for epidemics lasting weeks or months.

The rationale for our judgments as to how CHF should be defined was based on our knowledge of clinical practice in Quebec, the lack of standardization of medical practice, and the information required to provide an adequately accurate diagnosis. For example, the requirement of having two sequential diagnoses on the billing record to define CHF was based on usual clinical practice guidelines (e.g., Moe and Armstrong, 1988). Although these diagnoses are surrogates for actual positive tests, the universality of the drug plan in the elderly almost guarantees that we have the potential to identify all treated cases. During the period 1984–1993, diuretics were the drug of choice for most cases of CHF, although other pharmaceuticals were used, notably digoxin and angiotensin-converting-enzyme (ACE) inhibitors. We believe that the use of a combination of diagnostic codes and filled prescriptions for diuretics increased accuracy, although there would be some misclassification involved. Another strength of this methodology is that we made use of rendered services carried out both within and without hospital, so that they should in principal perform more accurately than simple hospital discharge summaries which provide, at best, a snapshot of acute illnesses or exacerbations of chronic ones and cause-of-death information, which is notoriously inaccurate for cardiovascular and respiratory diseases.

The positive association found for COH, a marker for carbon particles, is consistent with previous observations that inhaled urban particles can cause rapid and sustained elevations of levels of circulating plasma endothelin-1 and -3 (Bouthillier et al., 1998; Vincent et al., 2001). We hypothesize that ambient particles can affect the heart indirectly through a modification of pulmonary endothelin homeostasis. This is based partly on the findings that human subjects exposed to ambient $PM_{2.5}$ exhibit dose-dependent increases of levels of circulating endothelins (Vincent et al., unpublished observation). Endothelins are among the most potent vasoconstrictors known. Pulmonary release of endothelin-1 contributes to an elevation of plasma endothelin-1 and to vasoconstriction (Kjekshus et al., 2000) and plasma endothelin levels correlate with severity of disease in CHF and also predict cardiac death (Galatius-Jensen et al., 1996). Likewise, reduction of endothelin levels in CHF is associated with improvement of symptoms (Tsumamoto et al., 1995). Endothelins appear to be involved directly in the pathogenesis of cardiovascular diseases through their vasopressor and mitogenic mechanisms, and endothelin receptor antagonists are now being introduced in the treatment of CHF to reduce peripheral vascular and pulmonary resistance and to increase cardiac output (Giannessi et al., 2001; Spieker et al., 2001). Elevated circulating endothelins may also affect cardiac arrhythmia and dysrhythmia, enhance myocardial ischemia and promote infarct extension, and contribute to increased systemic and pulmonary vascular resistance, vascular dysfunction, and renal impairment in diabetes and chronic heart failure patients (Best and Lerman, 2000; Spieker et al., 2001; Zouridakis et al., 2001).

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