HEI

RESEARCH REPORT

HEALTH EFFECTS INSTITUTE

Number 97
October 2000

Final Version

Identifying Subgroups of the General Population That May Be Susceptible to Short-Term Increases in Particulate Air Pollution: A Time-Series Study in Montreal, Quebec

Mark S Goldberg, John C Bailar III, Richard T Burnett, Jeffrey R Brook, Robyn Tamblyn, Yvette Bonvalot, Pierre Ernst, Kenneth M Flegel, Ravinder K Singh, and Marie-France Valois

Includes a Commentary by the Institute's Health Review Committee

HEALTH
EFFECTS
INSTITUTE

The Health Effects Institute, established in 1980, is an independent and unbiased source of information on the health effects of motor vehicle emissions. HEI supports research on all major pollutants, including regulated pollutants (such as carbon monoxide, ozone, nitrogen dioxide, and particulate matter) and unregulated pollutants (such as diesel engine exhaust, methanol, and aldehydes). To date, HEI has supported more than 200 projects at institutions in North America and Europe and has published over 100 research reports.

Typically, HEI receives half its funds from the US Environmental Protection Agency and half from 28 manufacturers and marketers of motor vehicles and engines in the United States. Occasionally, funds from other public and private organizations either support special projects or provide resources for a portion of an HEI study. Regardless of funding sources, HEI exercises complete autonomy in setting its research priorities and in reaching its conclusions. An independent Board of Directors governs HEI. The Institute's Health Research and Review Committees serve complementary scientific purposes and draw distinguished scientists as members. The results of HEI-funded studies are made available as Research Reports, which contain both the Investigators' Report and the Health Review Committee's evaluation of the work's scientific quality and regulatory relevance.

HEI STATEMENT
Synopsis of Research Report 97

Identifying Subgroups of the General Population That May Be Susceptible to Short-Term Increases in Particulate Air Pollution

BACKGROUND

Epidemiologic analyses of mid-20th-century air pollution episodes such as the 1952 London Fog indicated that excess mortality was associated with elevated air pollution, and the excess mortality was concentrated among people with preexisting cardiovascular, and especially respiratory, diseases. More recently, smaller associations with mortality have been consistently reported at much lower air pollution levels. However, because these studies used routinely collected mortality data obtained from death certificates, few of the studies could describe in detail the clinical conditions of the decedents preceding their deaths. Therefore, studies that could address this issue were needed.

APPROACH

In 1994, HEI requested applications for studies that would provide more information on the conditions of individuals before death, to further understanding of the mortality–particulate matter association. Dr Mark Goldberg and his colleagues at McGill University in Montreal, Quebec, received funds to conduct a time-series study in Montreal, where data from the Quebec Health Insurance Plan were available, as well as mortality and air pollution data. Because of the comprehensive nature of this health insurance database, the investigators were able to link individual deaths in Montreal to medical information up to 5 years before death. These data were then used in conjunction with clinical expertise to define susceptible groups and to assess risk of death in those groups for three different indices of particulate matter. The investigators had two major objectives: (1) to determine whether concentrations of particles in the ambient air of Montreal were associated with daily all-cause and cause-specific mortality and (2) to determine whether groups of the population had higher than average risks of death from exposure to particles.

RESULTS AND INTERPRETATION

The investigators report total and specific causes of death associated with the average level of air pollution measured the same day and 2 days prior to death (a 3-day mean lag). Three measures of particulate matter were used: coefficient of haze (COH), total sulfate measured at the monitoring station in Sutton, Quebec (150 km southeast of Montreal), and a predicted estimate of particulate matter 2.5 μm or smaller in aerodynamic diameter ($PM_{2.5}$) that was calculated from daily COH, sulfate, and airport visibility data. Other particulate matter measures were analyzed and are in appendices available on request from the Health Effects Institute and from the HEI web site. For each of the three particle measures, the investigators reported an association with mortality from respiratory diseases and other nonaccidental deaths, including diabetes. Additionally, COH was associated with increases in cancer deaths in general and the subset of lung cancer deaths; sulfate measured at the Sutton site was associated with mortality from coronary artery disease and cardiovascular diseases. Positive associations for other underlying causes of death were not found. All associations were generally stronger among those 65 years of age and older.

Analyses were also conducted for three groups of health conditions present before death (cancer, cardiovascular diseases, and respiratory diseases). The effects of the three particle measures varied somewhat by subset of disease. Subjects with acute lower respiratory disease, congestive heart failure, and a combined group of any cardiovascular diseases died at higher rates for increases in each of the three particulate matter measures. Associations with COH and predicted $PM_{2.5}$ were reported for subjects with cancer, chronic coronary artery disease, and any coronary artery disease, and effects of sulfate were shown for those with acute and chronic upper respiratory disease. No associations with the three measures of particulate matter were

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI from July 1995 to June 1999 and conducted by Dr Mark S Goldberg and colleagues of McGill University, Montreal, Canada. The following Research Report contains both the detailed Investigators' Report and a Commentary on the study prepared by the Institute's Health Review Committee.

observed for those with airways disease, acute coronary artery disease, or hypertension.

Dr Goldberg and colleagues have made a unique effort to address some of the limitations of mortality outcomes data that have been used in most earlier studies of air pollution and daily mortality. Their study has advanced current methods and scientific understanding in several ways through the linkage of a provincial insurance database with mortality and air pollution databases. The results suggest that persons with certain preexisting cardiac or respiratory conditions are at short-term increased risk of mortality due to ambient particulate matter. Observed apparent discrepancies between results using case definitions based on the Quebec Health Insurance Plan data and those using the more conventional death certificate information should be more thoroughly explored. Also, some other clinical conditions were identified for a possible association with increased risk of mortality. In particular, the investigators identified persons with cancer or diabetes, as well as those who had not received medical services in the year before death, as being at an increased risk of death. These results merit additional investigation.

Further analyses with this data set could advance understanding of who might be at greatest risk of mortality at levels of air pollution currently observed in the cities with relatively low air pollution levels.

Library of Congress Catalog Number for the HEI Report Series: WA 754 R432.
The paper in this publication meets the minimum standard requirements of the ANSI Standard Z39.48-1984 (Permanence of Paper) effective with Report 21, December 1988, and with Reports 25, 26, 32, 51, 65 Parts IV, VIII, and IX, and 91 excepted. These excepted Reports are printed on acid-free coated paper.

CONTENTS

Research Report 97

HEALTH EFFECTS INSTITUTE

Identifying Subgroups of the General Population That May Be Susceptible to Short-Term Increases in Particulate Air Pollution: A Time-Series Study in Montreal, Quebec

Mark S Goldberg, John C Bailar III, Richard T Burnett, Jeffrey R Brook, Robyn Tamblyn, Yvette Bonvalot, Pierre Ernst, Kenneth M Flegel, Ravinder K Singh, and Marie-France Valois

McGill University, Montreal, Quebec; University of Quebec, Laval, Quebec; University of Chicago, Chicago, Illinois; Health Canada, Toronto, Ontario; Environment Canada, Toronto, Ontario; and Public Health Department, Montreal, Quebec

Continued

COMMENTARY Health Review Committee

The Commentary about the Investigators' Report is prepared by the HEI Health Review Committee and staff. Its purpose is to place the study into a broader scientific context, to point out its strengths and limitations, and to discuss the remaining uncertainties and the implications of the findings for public health.

RELATED HEI PUBLICATIONS

Publishing History: This document was posted as a preprint on *www.healtheffects.org* and then finalized for print.

Citation for whole report:

Goldberg MS, Bailar JC III, Burnett RT, Brook JR, Tamblyn R, Bonvalot Y, Ernst P, Flegel KM, Singh RK, Valios M-F. 2000. Identifying Subgroups of the General Population That May Be Susceptible to Short-Term Increases in Particulate Air Pollution: A Time-Series Study in Montreal, Quebec. Research Report 97. Health Effects Institute, Cambridge MA.

When specifying a section of this report, cite it as a chapter of this document.

PREFACE

In 1994, HEI initiated a research program to investigate the complex issues associated with the health effects of exposure to particulate matter (PM)* in the air. This program was developed in response to growing concern about the potential public health significance of reported associations between daily fluctuations in levels of PM and changes in daily morbidity and mortality in time-series epidemiology studies. These results were questioned for a variety of reasons, including the lack of support from experimental studies and the lack of a mechanism to explain how such effects would occur. To address these issues HEI undertook two research initiatives in 1994: (1) the Particle Epidemiology Evaluation Project (Samet et al 1995, 1997), which evaluated six of the time-series epidemiology studies that had reported effects of PM on mortality; and (2) a program of toxicologic and epidemiologic studies (funded from RFA 94-2, "Particulate Air Pollution and Daily Mortality: Identification of Populations at Risk and Underlying Mechanisms"), which aimed to understand better how PM might cause toxicity and what factors might affect susceptibility. In all, HEI has issued five requests for research on PM and funded 34 studies or reanalyses over the last five years.

This Preface provides general regulatory and scientific background information relevant to studies funded from RFA 94-2, including the study by Mark Goldberg that is described in the accompanying Report and Commentary. All of the studies from RFA 94-2 have been completed and are either under review by HEI or have been published. The *HEI Program Summary: Research on Particulate Matter* (Health Effects Institute 1999) provides information on studies funded since 1996.

BACKGROUND

Particulate matter is the term used to define a complex mixture of anthropogenic and naturally occurring airborne particles. The size, chemical composition, and other physical and biological properties of PM depend on the sources of the particles and the changes the particles undergo in the atmosphere. In urban environments, these particles derive mainly from combustion, including mobile sources such as motor vehicles and stationary sources such as power plants. The most commonly used descriptor of particle size is *aerodynamic diameter*. Based on this parameter, ambient particles tend to fall into three size classes (often defined as modes): ultrafine or nuclei mode (particles less than 0.1 μm in diameter); fine or accumulation mode (particles between 0.1 and 2.5 μm in diameter), and coarse (particles larger than 2.5 μm in diameter). Fine and ultrafine particles are dominated by emissions from combustion processes while coarse particles are mostly generated by mechanical processes from a variety of noncombustion sources. Generally, the ultrafine and fine fractions are composed of carbonaceous material, metals, sulfate, nitrate and ammonium ions. The coarse fraction is composed mostly of mechanically generated particles and consists of insoluble minerals and biologic aerosols, with smaller contributions from primary and secondary aerosols and sea salts (US Environmental Protection Agency [EPA] 1996).

A number of early epidemiologic studies indicated that human exposure to high concentrations of PM, such as London fog, had deleterious effects (such as increased number of deaths), particularly in children, the elderly, and those with cardiopulmonary conditions (Firket 1931; Logan 1953; Ciocco and Thompson 1961; Gore and Shaddick 1968). Because of this apparent relation to increased mortality, the EPA has regulated the levels of ambient PM since 1971, when the Clean Air Act was first promulgated. This act authorized the EPA to set National Ambient Air Quality Standards (NAAQSs) for a number of potentially harmful air pollutants (including PM) in order to protect the health of the population, particularly those thought to be sensitive.

The first NAAQS for PM was based on controlling total suspended PM or particles up to 40 μm in diameter. In 1978, the standard was revised to regulate inhalable particles, or particles than can deposit in the respiratory tract and therefore have greater potential for causing adverse health effects. These are particles with an aerodynamic diameter of 10 μm or less (PM_{10}). More recent epidemiologic studies, published in the early 1990s, indicated a relatively consistent association between small short-term increases in PM levels and increases in both mortality and morbidity from respiratory and cardiovascular diseases (reviewed by the Committee of the Environmental and Occupational Health Assembly, American Thoracic Society [Bascom et al 1996]).

Some studies also suggested that long-term exposure to low levels of PM is associated with adverse effects (Dockery et al 1993; Pope et al 1995). These latter studies also pointed to a possible role of fine particles (less than

* A list of abbreviations and other terms appears at the end of the Investigators' Report.

Table 1. Current NAAQSs for PM (set in 1997)

	PM_{10}	$PM_{2.5}$
Daily Standard	150 μg/m^3	65 μg/m^3
Annual Standard	50 μg/m^3	15 μg/m^3

2.5 μm in aerodynamic diameter [$PM_{2.5}$]). In 1997, the EPA considered the evidence for the effects of fine particles sufficient to promulgate a fine particle standard while retaining the PM_{10} standard (US Environmental Protection Agency 1997) (see Table 1). The next review of the PM NAAQS is scheduled to be completed by the year 2002.

RESEARCH PROGRAM FROM HEI RFA 94-2

The wealth of epidemiologic data published in the early 1990s suggested an association between PM and health effects, but aspects of these findings were not well understood. Problems involved uncertainties in the exposure estimates, confounding by weather or other factors, the role of copollutants, and the mechanisms by which particles may cause effects. Moreover, although the epidemiologic findings were consistent across different communities exposed to distinct mixes and levels of pollutants, they were not well supported by either human chamber studies or animal inhalation studies aimed at delineating pathologic changes that might result in death. Failure of the experimental studies to provide support for the epidemiologic findings was attributed to insufficient statistical power, use of particles not representative of ambient particles, or use of animals not representative of the individuals susceptible to increased mortality.

By the mid 1990s, it became apparent that the research to advance our understanding of the association between exposure to particles and daily mortality found in the epidemiologic studies needed to focus on identifying (1) susceptible populations, (2) mechanisms by which particles may lead to increased mortality, and (3) characteristics of the particles responsible for the effects. It was recognized that both epidemiologic and experimental studies would be required.

The HEI program initiated in 1994 was aimed at addressing these research needs. Six epidemiologic and toxicologic studies were funded through RFA 94-2, and three additional studies were added through the preliminary application process. As a group, the five epidemiologic studies investigated: (1) social and medical factors that might increase the risk of mortality when particulate pollution increases (Mark Goldberg, this report); (2) components of particulate pollution that might account for its effect on mortality (Morton Lippmann of the New York University School of Medicine [see Lippmann et al 2000] and Erich Wichmann of the GSF Insitute of Epidemiology and Ludwig Maximilian University); and (3) cause of death (Harvey Checkoway of the University of Washington and Mark Goldberg) or possible pathophysiologic mechanisms that might lead to death in people exposed to particulate air pollution (Douglas Dockery of Harvard School of Public Health [see Dockery et al 1999]).

The four experimental studies tested the hypothesis that older animals or animals with preexisting lung or heart disease or respiratory infections are more sensitive to the acute effects of particles than healthy animals. They investigated possible mechanisms leading to mortality such as inflammation, changes in immune response, or changes in cardiac and respiratory function. Three of these studies used for the first time concentrated ambient particles (CAPs) (John Godleski of Harvard School of Public Health [see Godleski et al 2000], and Terry Gordon [see Gordon et al 2000] and Judith Zelikoff of New York University School of Medicine). In these CAPs studies, particles in the range of about 0.1 to 2.5 μm are concentrated while those greater than 2.5 μm are removed and those under 0.1 μm remain at the ambient concentration. CAPs exposures represent a significant fraction of ambient PM and provide a reasonable approach to mimicking the exposure to PM in epidemiology studies. The fourth experimental study (Günter Oberdörster, University of Rochester School of Medicine and Dentistry) focused on evaluating the effects of different ultrafine particles that have been hypothesized to be more toxic than fine particles (see Oberdörster et al 2000).

CONTINUING RESEARCH

Many of the key questions identified in the early 1990s are still relevant and much research is ongoing to address them. The research strategies have evolved, however, as results from previous studies have provided insights into which animal models and which endpoints may be the most helpful to evaluate. In addition, advances in exposure assessment and statistical methods have pointed to new approaches for conducting epidemiologic studies. Since RFA 94-2, HEI has funded a number of research projects that build on the new findings and approaches. These studies will be completed by the end of 2002.

REFERENCES

Bascom R, Bromberg PA, Costa DA, Devlin R, Dockery DW, Frampton MW, Lambert W, Samet JM, Speizer FE, Utell M. 1996. Health effects of outdoor air pollution. Part 1. Am J Respir Crit Care Med 153:3–50.

Ciocco A, Thompson DJ. 1961. A follow-up on Donora ten years after: Methodology and findings. Am J Pub Health 15:155–164.

Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG, Speizer FE. 1993. An association between air pollution and mortality in six US cities. N Engl J Med 329:1753–1759.

Dockery DW, Pope CA III, Kanner RE, Villegas GM, Schwartz J. 1999. Daily Changes in Oxygen Saturation and Pulse Rate Associated with Particulate Air Pollution and Barometric Pressure. Research Report 83. Health Effects Institute, Cambridge MA.

Firket J. 1931. The cause of the symptoms found in the Meuse Valley during the fog of December 1930. Bull Acad R Med Belg 11:683–741.

Godleski JJ, Verrier RL, Koutrakis P, Catalano P. 2000. Mechanisms of Morbidity and Mortality from Exposure to Ambient Air Particles. Research Report 91. Health Effects Institute, Cambridge MA.

Gordon T, Nadzieko C, Chen LC, Schlesinger R. 2000. Effects of Concentrated Ambient Particles in Rats and Hamsters: An Exploratory Study. Research Report 93. Health Effects Institute, Cambridge MA.

Gore AT, Shaddick CW. 1968. Atmospheric pollution and mortality in the county of London. Br J Prev Soc Med 12:104–113.

Health Effects Institute. 1999. Research on Diesel Exhaust (HEI Research Program Summary). Health Effects Institute, Cambridge MA.

Health Effects Institute. 1999. Research on Particulate Matter (HEI Research Program Summary). Health Effects Institute, Cambridge MA.

Lippmann M, Ito K, Nádas A, Burnett RT. 2000. Association of Particulate Matter Components with Daily Mortality and Morbidity in Urban Populations. Research Report 95. Health Effects Institute, Cambridge MA.

Logan WPD. 1953. Mortality in London fog incident. Lancet i:336–338.

Oberdörster G, Finkelstein JN, Johnston C, Gelein R, Cox C, Baggs R, Elder ACP. 2000. Acute Pulmonary Effects of Ultrafine Particles in Rats and Mice. Research Report 96. Health Effects Institute, Cambridge MA.

Pope CA III, Thun MJ, Namboodiri MM, Dockery DW, Evans JS, Speizer FE, Heath CW. 1995. Particulate air pollution as a predictor of mortality in a prospective study of US adults. Am J Respir Crit Care Med 151:669–674.

Samet JM, Zeger SL, Birhane K. 1995. The association of mortality and particulate air pollution. In: Particulate Air Pollution and Daily Mortality: Replication and Validation of Selected Studies, The Phase I.A Report of the Particle Epidemiology Evaluation Project. Health Effects Institute, Cambridge MA.

Samet JM, Zeger SL, Kelsall JE, Xu J, Kalkstein LS. 1997. Air pollution, weather, and mortality in Philadelphia. In: Particulate Air Pollution and Daily Mortality: Analysis of the Effects of Weather and Multiple Air Pollutants, The Phase I.B Report of the Particle Epidemiology Evaluation Project. Health Effects Institute, Cambridge MA.

US Environmental Protection Agency. 1996. Air Quality Criteria for Particulate Matter. Vol I. Document EPA/600/P-95/001. Office of Research and Development, Washington DC.

US Environmental Protection Agency. 1997. Revisions to the National Ambient Air Quality Standards for particulate matter: Final rule. Fed Regist 52:24634–24669.

INVESTIGATORS' REPORT

Identifying Subgroups of the General Population That May Be Susceptible to Short-Term Increases in Particulate Air Pollution: A Time-Series Study in Montreal, Quebec

Mark S Goldberg, John C Bailar III, Richard T Burnett, Jeffrey R Brook, Robyn Tamblyn, Yvette Bonvalot, Pierre Ernst, Kenneth M Flegel, Ravinder K Singh, and Marie-France Valois

ABSTRACT

This study was undertaken in order to shed light on which groups of the general population may be susceptible to the effects of ambient particles. The objectives of the study were (1) to determine whether concentrations of particles in the ambient air of Montreal, Quebec, were associated with daily all-cause and cause-specific mortality in the period 1984 to 1993, and (2) to determine whether groups of the population had higher than average risks of death from exposure to particles.

From the network of fixed-site air pollution monitors in Montreal we obtained daily mean levels of various measures of particles, gaseous pollutants, and weather variables measured at Dorval International Airport. We also used measurements of sulfate from an acid rain monitoring station 150 km southeast of the city (Sutton, Quebec). We estimated associations for particulate matter (PM)* with an aerodynamic diameter of 10 μm or smaller (PM_{10}), or 2.5 μm or smaller ($PM_{2.5}$), total suspended particles (TSP), coefficient of haze (COH), an extinction coefficient, and sulfate. Because substantial data for fine particles were missing, we developed a regression model to predict $PM_{2.5}$ and to predict sulfate from $PM_{2.5}$. In the main body of the report, we present results for COH, predicted $PM_{2.5}$, and sulfate. Detailed results for all pollutants are included in Appendices H through O, which are available on request from Health Effects Institute and from the HEI web site at *www.healtheffects.org*.

To address the first objective, we made use of the underlying causes of death among all 140,939 residents of Montreal who died between 1984 and 1993. We regressed the logarithm of daily counts of cause-specific mortality on the daily mean levels for a variety of measures of particles, accounting for seasonal and subseasonal fluctuations in the mortality time series, overdispersion, and weather factors.

To address the second objective, we developed algorithms to define conditions that subjects had prior to death, with the focus on cardiopulmonary diseases. These algorithms were based on information retained on the databases of the universal Quebec Health Insurance Plan (QHIP). The databases include records of all procedures (eg, type of surgery), physician visits, and consultations carried out by all physicians in Quebec. For persons ≥ 65 years and for all recipients of social assistance the prescription database contains records of all pharmaceuticals dispensed (type of medication, dose, quantity). For each group of conditions defined, we used the same statistical model that was used in the analyses of all nonaccidental causes of death.

In the analyses of cause-specific mortality, we found evidence of associations for all nonaccidental causes of death and specific causes of death—cancer, coronary artery disease, respiratory diseases, and diabetes—that were consistent across most metrics of ambient air particle concentrations, evaluated as the 3-day mean of particle concentrations measured on the day of death (lag 0) and on each of the two days before death (lag 1, lag 2). Associations for all cardiovascular diseases combined were found only with sulfate. As well, we generally found increased daily mortality for persons 65 years of age and over. The results for all nonaccidental causes of death are similar to findings from other studies; the mean percent increase in mortality for a 100 $\mu g/m^3$ increase in daily TSP at lag 0 was 6.7%.

In the analyses of the groups defined from the QHIP data, there was little evidence of associations with air pollutants among persons who before death were classified

*A list of abbreviations and other terms appears at the end of the Investigators' Report.

This Investigators' Report is one part of Health Effects Institute's Research Report 97, which also includes a Preface, a Commentary by the Health Review Committee, and an HEI Statement about the research project. Correspondence concerning the Investigators' Report may be addressed to Dr Mark S Goldberg, Epidemiology and Biostatistics Unit, Research Centre on Human Health, INRS-IAF, University of Quebec, 531 Boulevard de Prairies, Laval, Quebec, Canada H7V 1B7.

Although this document was produced with partial funding by the United States Environmental Protection Agency under Assistance Award R824835 to the Health Effects Institute, it has not been subjected to the Agency's peer and administrative review and therefore may not necessarily reflect the views of the Agency, and no official endorsement by it should be inferred. The contents of this document also have not been reviewed by private party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views or policies of these parties, and no endorsement by them should be inferred.

as having acute or chronic upper respiratory diseases, airways diseases, hypertension, acute coronary artery diseases, and cerebrovascular diseases. On the other hand, we found consistent increases across most types of ambient particles for persons who had cancer, acute lower respiratory diseases, any form of cardiovascular disease, chronic coronary artery diseases, and congestive heart failure. As well, we found an association for individuals who did not have any cardiovascular disease, lower respiratory diseases, and cancer. This latter group consisted of persons who had no interactions with the health care system one year before death (12%) and individuals with a wide variety of potentially fatal diseases (52%), including neurological conditions (12%), diabetes (8%), cardiac dysrhythmias (8%), dementia (6%), organic psychotic disorders (6%), and anemias (4%).

As statistical power was reduced in the analyses presented above, differences between groups (eg, < 65 and ≥ 65 year age groups) were not usually statistically significant. The association with diabetes has not been reported previously, and this needs to be replicated in other studies. These results suggest that certain groups of the population may be susceptible to the effects of airborne particles; data for a few of these groups, notably congestive heart failure and acute lower respiratory diseases, are consistent with some prevailing hypotheses.

INTRODUCTION

The air pollution episode in London in the winter of 1952 demonstrated conclusively that very high levels of ambient particle air pollution can cause immediate and dramatic increases in mortality (Logan 1953; Boyd 1960). This episode was caused by cold, stagnant weather conditions that trapped combustion products (particles and gases) at ground level. The smog that was produced increased respiratory and cardiovascular mortality, especially in the elderly. Other major air pollution episodes in the Meuse Valley in Belgium (Firket 1936) and in Donora, Pennsylvania (Shrenk et al 1949; Ciocco and Thompson 1961), were associated with health effects similar to those that occurred in London.

In the 1950s, the levels of air pollution in most North American and European cities were 10 to 50 times higher than those found today. New emission control technologies, such as catalytic converters in automobiles, have contributed to reducing levels of particles and other pollutants over the years, despite an increased amount of combustion from industrial, commercial, and personal activities. For example, in the US during the period 1986 to 1995, mean annual emissions and ambient concentrations of particles with an aerodynamic diameter under 10 micrometers (PM_{10}) decreased by 22% and 17%, respectively (US Environmental Protection Agency [EPA] 1996); annual emissions and ambient concentrations of sulfur dioxide (SO_2) have decreased on average by 18% and by 37%, respectively.

Despite the general reduction in pollution levels, recent studies have shown that concentrations of ambient air particles are associated with a wide range of effects on human health, including increased hospitalization for respiratory disease (Pope 1989a,b; Lipfert and Hammerstrom 1992; Thurston et al 1992, 1993; Burnett et al 1994; Schwartz 1994a,b); emergency room visits for respiratory illness (Samet et al 1981; Sunyer et al 1993; Delfino et al 1997); exacerbation of episodes of asthma (Whittemore and Korn 1980; Bates et al 1990; Ostro et al 1991; Pope and Dockery 1992; Roemer et al 1993); increased incidence and duration of respiratory symptoms (Braun-Fahrlander et al 1992; Hoek and Brunekreef 1993; Roemer et al 1993); decrements in lung function (Dockery et al 1982; Chestnut et al 1991; Pope et al 1991; Hoek and Brunekreef 1993, 1994; Koenig et al 1993; Pope and Kanner 1993); restricted activity of adult workers, and increases in absences of children from elementary school (Ostro 1983, 1987, 1990; Ostro and Rothschild 1989; Ransom and Pope 1992); and increased mortality (Schwartz 1991, 1993, 1994a,b,c,d; Dockery et al 1992; Pope et al 1992; Schwartz and Dockery 1992; Ito et al 1993; Kinney et al 1995; Moolgavkar et al 1995; Saldiva et al 1995; Samet et al 1995; Styer et al 1995; Anderson et al 1996a; Bacharova et al 1996; Ballester et al 1996, 1997; Ito and Thurston 1996; Ostro et al 1996; Rahlenbeck et al 1996; Schwartz et al 1996; Spix and Wichmann 1996; Sunyer et al 1996; Touloumi et al 1996; Verhoeff et al 1996; Zmirou et al 1996; Borja-Aburto et al 1997; Michelozzi et al 1998).

In addition, three large cohort studies that followed thousands of subjects prospectively have been published (Abbey et al 1991, 1993, 1995; Dockery et al 1993; Pope et al 1995). The Harvard Six Cities Study (Dockery et al 1993) and the American Cancer Society's Cancer Prevention Study–II (Pope et al 1995) have reported estimated increases in annual average total mortality associated with fine particles. The Seventh-Day Adventist Health Study (Abbey et al 1991, 1993, 1995) showed increases in respiratory diseases associated with exposure to TSP and PM_{10}, although no associations with mortality have been found (Abbey et al 1999). Because the findings of the Harvard Six Cities Study and the American Cancer Society Study have been questioned on methodological grounds, particularly regarding possible residual confounding, errors in exposure, and robustness of the results to changes

in the specification of the statistical models, a reanalysis of these studies has been conducted under the auspices of the Health Effects Institute (2000).

The results of the times series studies for all causes of death are remarkably consistent, as is evidenced by a recent meta-analysis (Schwartz 1994a) of nine US studies (Fairley 1990; Kinney and Özkaynak 1991; Schwartz 1991; Dockery et al 1992; Pope et al 1992; Schwartz and Dockery 1992; Schwartz 1993) and one in London, England (Schwartz and Marcus 1990), that showed that daily mortality increased from about 4% to 9% per each 100 $\mu g/m^3$ increase in TSP, with a summary estimate of 6% (95% confidence interval [CI]: 4%–6%). Similar results have been found in most studies conducted since this meta-analysis was published. (As well, many of the American time-series studies have been reanalyzed and were consistent with the published results [Samet et al 1995].) This consistency in the slope of the exposure-response function could be due to either a true identified and possibly causal association or to undetected biases that are common to all of these studies (Goldberg 1996).

A number of authors (Bates 1992; Seaton et al 1995; Goldberg 1996; Frank and Tankersley 1997) have suggested that only persons in poor health should be affected by the relatively low levels of air pollution present today. Several hypotheses have been put forward:

- among persons with myocardial damage, exposure to acid aerosols or ozone (O_3) may increase lung permeability and lead to pulmonary edema or to inflammation in damaged areas of the lung (Bates 1992);
- among persons with cardiac disease, exposure to air pollutants may cause acute pulmonary disease, such as bronchiolitis or pneumonia, thereby leading to congestive heart failure (Bates 1992);
- among 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 (Seaton et al 1995); and
- among persons in poor and failing health (usually with some serious systemic disease), loss of homeostasis will increase susceptibility to external insults, such as air pollution (Frank and Tankersley 1997). A consequence of this last hypothesis is that individuals with systemic diseases (eg, cancer, diabetes, renal disease) may be susceptible to the short-term effects of air pollution.

It is critically important to identify groups at higher than average risk of dying from the short-term effects of particle air pollution. In terms of public health, uncertainties regarding vulnerable populations impede regulators in formulating effective policies to manage air pollution. From the scientific perspective, despite the widespread consistency in the observed effects, the data are insufficient to determine whether the association with particle air pollution and daily mortality is causal. Such a determination cannot be made without first identifying susceptible groups, as it is implausible that all persons are at risk for the adverse effects of short-term air pollution. Toxicology can provide some answers to this thorny question, but epidemiological data may be the most persuasive as they are based on actual conditions in existing populations. As well, epidemiology is well placed to address and evaluate which, if any, of the above hypotheses, or some combination of these, may approximate the truth. These data could then inform which toxicologic models are the most appropriate, and these models could then lead to further characterization of causal mechanisms.

This epidemiological study is the first to address specifically the issue of identifying susceptible populations. This study had two objectives:

1. to determine whether concentrations of particles in the ambient air of Montreal, Quebec, were associated with daily all-cause and cause-specific mortality in the period 1984 to 1993, inclusive; and
2. to identify groups of the general population with specific health conditions prior to death who were susceptible to the effects of increased levels of ambient particles.

OVERVIEW OF THE REPORT

The report is presented in three parts. In Part 1, we describe our research methods to estimate the magnitude of the association between concentrations of ambient particles and daily all-cause and cause-specific mortality. In Part 2, we describe the methods and results of the time-series analyses to define potentially susceptible groups of the study population. In Part 3, we present a discussion of the results from these two sets of analyses.

The target population was all residents of the Island of Montreal (hereafter referred to as Montreal) during the period 1984 to 1993. We considered deaths among residents of Montreal who died in the city during this time. Decedents in the target population were identified from the computerized provincial vital statistics register. The unit of observation therefore is the day. In the first part of the report, we describe time-series analyses of the association between daily cause-specific mortality and daily levels of

ambient particles (as estimated from fixed-site monitoring stations in the city).

In the second part, we describe the construction of a set of indicators of disease group used to identify persons having specific conditions prior to death. These conditions included respiratory diseases, cardiovascular illnesses, and cancer. For each decedent, we used Quebec's universal health insurance system, QHIP, to obtain medical information prior to death. The QHIP provides details of interactions with the Quebec health care system, including types of services rendered, physician visits, diagnoses, and drug prescriptions (Figure 1). Using these data, we developed algorithms to define subjects who had specific medical conditions before death. We then conducted time-series analyses within each group separately to estimate the association between daily mortality and particles.

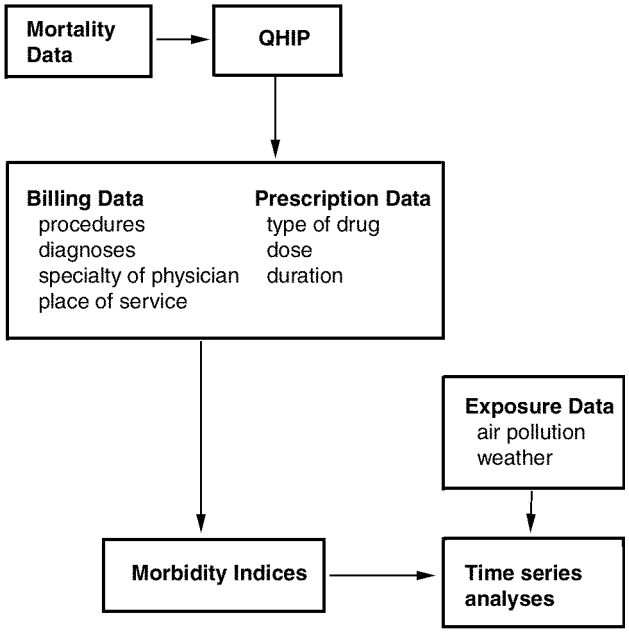

Figure 1. Flow chart for project. The analyses of cause-specific mortality using standard methods for time series, as presented in Part 1 of this report, are represented by the boxes in the top left corner and the two boxes in the lower right corner of the figure. The definition of groups with specific medical conditions prior to death, as described in Part 2, was based on algorithms that we developed to use billing and prescription data from the QHIP 5 years prior to death. We then conducted separate analyses of

PART 1: THE ASSOCIATION BETWEEN CAUSE-SPECIFIC MORTALITY AND AMBIENT PARTICLES IN MONTREAL, 1984 TO 1993

MATERIALS AND METHODS

Data Sources

The data sources (Table 1) include weather data collected routinely at Environment Canada's observatory at Dorval International Airport located in the western part of the island of Montreal, daily measurements of environmental

Table 1. Summary of Original Data Files

Database	Description of Contents
Weather database	Air temperature, barometric pressure, dew point temperature, wind direction, visibility (at Dorval International Airport)
Environmental databases (Environment Canada, Canadian Air and Precipitation Monitoring Network, and the Montreal Urban Community)	Particulate pollutants (measures of TSP, COH, PM_{10}, $PM_{2.5}$, SO_4^{2-}), and gaseous pollutants (NO, NO_2, CO, CO_2, SO_2, O_3)
Quebec mortality database	Identifying information (names, birth date, sex), underlying cause of death (ICD-9), date and place of death
QHIP database	Mortality, sociodemographic factors (eg, age), usual place of residence, billings by physicians for services, drug prescriptions (≥65 years old and recipients of social assistance), and selected procedures carried out in hospitals, emergency rooms, and outpatient clinics
Quebec hospital discharge database	Hospital discharge diagnoses (ICD-9) that contributed to length of stay, discharge destination (such as home, other institutions, morgue), date of admission and discharge, length of stay, sociodemographic factors

particles at fixed monitoring stations, and hourly measurements of gaseous pollutants (carried out by the Montreal Urban Community [MUC] and the National Air Pollution Surveillance Program of Environment Canada [NAPS]), mortality data retained by the Quebec Minister of Health and Social Services, Quebec health insurance data administered by the QHIP, and Quebec hospital discharge data.

Weather Data The weather data consisted of daily visibility data, barometric pressure, temperature, total precipitation (distinguishing snow from rain), relative humidity, and dew point temperature. The visibility data were obtained using hourly sightings from ground level at the airport to discrete targets located at <3.2, 3.2, 4.8, 5.6, 6.4, 8.8, 9.3, 20.9, and 72.4 km distant.

Pollutant Data Environmental measurements of particulate matter and gaseous pollutants in Montreal that were used in the study are summarized in Table 2. Most measurements were carried out by the MUC, although the

Table 2. Particulate Matter and Gaseous Pollutant Data[a] Used in Statistical Analyses, Montreal, 1984 to 1993

Pollutant	Start Year	Number of Sites	Duration	Frequency	Samplers Used	Analytic Methods
TSP	1984	19	24 Hour	Every 6th day	High-volume samplers (flow rate 1.5 m^3/min); midnight to midnight	Washed glass filters, mass measured on Sartorius AC121S digital electronic balance
Sulfate from TSP	1984	13	24 Hour	Every 6th day	High-volume samplers (1.5 m^3/min); midnight to midnight	Soluble sulfate on filters extracted by hot water and analyzed by ionic chromatography
PM_{10}	1984	2	24 Hour	Every 6th day	Sierra-Anderson dichotomous samplers (flow rate 16.7 L/min); midnight to midnight	Electronic microbalance at constant temperature and relative humidity
Sulfate from PM_{10}	1984	2	24 Hour	Every 6th day	High-volume samplers	Dionex ion chromatography
$PM_{2.5}$	1984	2	24 Hour	Every 6th day	Sierra-Anderson dichotomous samplers (flow rate 16.7 L/min)	Electronic microbalance at constant temperature and relative humidity
Sulfate from $PM_{2.5}$	1984	2	24 Hour	Every 6th day	Same as $PM_{2.5}$	Dionex ion chromatography
COH	1984	11	Hourly	Continuous; 2-hr integrated sampling	AISI Sequential (RAC)[b], using continuous roll of white filter paper (flow rate 0.4 m^3/hr)	Opacity as measured by photometer, in COH units/0.8 m^3 of air
Total sulfate from Sutton monitoring station	1986	1	24 Hour	Daily	Downward-facing, open-faced filterpack mounted at 10 m; 25 m^3/min mass flow controlled; 8 am to 8 am sampling	Dionex ion chromatograph
SO_2	1984	13	Hourly	Continuous	Philips 9700, Monitor Lab 8850	(1) ultraviolet fluorescence and (2) electrical conductivity from changes in chemical composition of a bromine solution
O_3	1984	9	Hourly	Continuous	Bendix 8002	Chemiluminescence
NO	1984	8	Hourly	Continuous	Thermo Electron 14B	Chemiluminescence
NO_2	1984	8	Hourly	Continuous	Thermo Electron 14B	Chemiluminescence
CO	1984	12	Hourly	Continuous	Thermo Electron 48	Infrared absorption

[a] PM was measured by Environment Canada as part of the National Air Pollution Surveillance Program. All other pollutants measured by the Montreal Urban Community. The number of sites changed during the study period. All gaseous pollutants, sulfate from Sutton, and COH were measured daily from the start date; PM and TSP were measured irregularly (although based approximately on an every-6-day schedule).

[b] AISI = American Iron and Steel Institute; RAC = Research Appliance Corporation.

majority of the PM_{10} and all of the $PM_{2.5}$ measurements, which came from two monitoring stations in Montreal, were part of NAPS and the Canadian Acid Aerosol Measurement Program (CAAMP) of Environment Canada (Brook et al 1997a,b).

We also used daily sulfate measurements for the period 1986 to 1993 from the Canadian Air and Precipitation Monitoring Network (CAPMoN) station near Sutton, Quebec, a rural community about 150 km southeast of the city (Figure 2). There were two reasons for using this station. First, daily observations of sulfate, $PM_{2.5}$, and PM_{10} in Montreal did not cover the entire study period, so alternate data were needed. Second, because the regional component of sulfate and particles is influenced from long-range transport of pollutants, measurements of sulfate at the Sutton station represent background levels of particle air pollution influencing southwest Quebec, including Montreal (Brook et al 1997b).

COH and the criteria gaseous pollutants were also measured daily. COH was measured at various monitoring stations using two-hour integrated samples, and mean daily values were calculated for each monitor and then averaged across the city. The data for COH, an excellent indicator of ambient carbon (see below), thus represented our only measure of daily particles. Mean daily values for the gaseous pollutants were similarly calculated. PM_{10}, $PM_{2.5}$, and sulfate were measured about every six days at two Montreal locations (Ontario Street and Duncan Street) from 1984 to 1993 using Sierra-Anderson dichotomous samplers (Brook et al 1997b). As part of the CAAMP, this measurement schedule was increased to daily sampling at one site (Ontario Street) from July 1992 to September 1995 (Brook et al 1997b). Daily measurements of PM_{10} and $PM_{2.5}$ were also made with dichotomous samplers, while daily sulfate data were obtained using an annular denuder/filterpack system (Koutrakis et al 1988). Measurements of sulfate at Sutton were made daily using open-faced filterpacks and, as with the other two Environment Canada programs mentioned above, concentrations of sulfate were estimated by ion chromatography. Although we monitored for acid aerosols, we did not have the opportunity to analyze these data.

Most pollutants were measured in MUC laboratories using EPA-approved methods. The major monitoring stations, generally those in which criteria pollutants were measured, were included in the NAPS database. Environment Canada regularly audited these stations for the gaseous pollutants. Prior to archiving the data in provincial and national environment databases, standard quality assurance tests were undertaken, such as tests for outliers and examinations of intersite correlations.

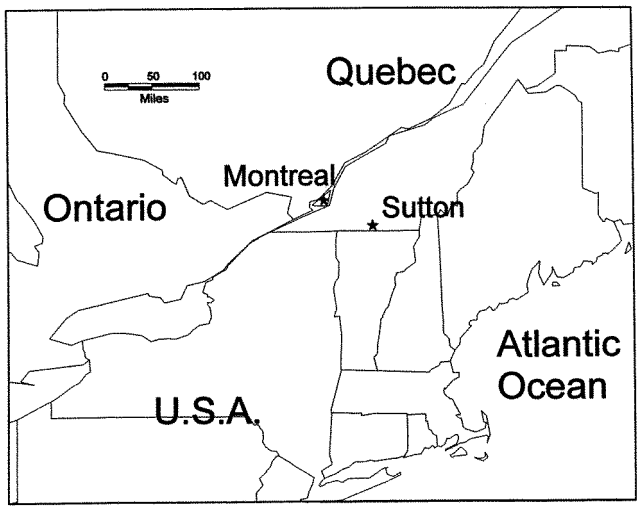

Figure 2. Study sites. All residents of the island of Montreal from 1984 to 1993 were the study population. The study focused on Montreal residents who died in the city during this time. Data were available from sampling stations in the city and at Dorval International Airport, including PM gaseous pollutants, and haze pollutants. Sulfate data were available from an additional station at Sutton, Quebec, about 150 km southeast of Montreal.

Environment Canada was responsible for measurements of PM and sulfate derived from PM (Table 2). The quality assurance procedures followed for the dichotomous sampler measurements were described by Brook and colleagues (1997a). Quality of the sulfate measurements was examined through regular testing of blanks, periodic calibration of mass flow controllers, and intercomparison with other networks (eg, CAAMP sulfate, EPA CastNet sulfate). Precision was determined through short-term special studies carried out at selected locations.

We used the visibility data to calculate an extinction coefficient, which represents the amount of absorption and scattering by particles. We used visibility data recorded at noon unless there was precipitation (snow or rain). In the event of inclement weather, we first searched the data in the afternoon for an initial sighting in which there was fair weather; if no estimate of visibility could be found, we then searched the data for the morning of the same day, starting at noon, for valid sightings. We then converted visibility into an extinction coefficient after accounting for relative humidity, through the relationship [3.91/visual range (km)] × f(relative humidity), where f is an empirical function of relative humidity (Özkaynak et al 1985; Kinney and Özkaynak 1991; Delfino 1994). About 80% of the visibility data were derived from measurements made at noon, with other hours of the day (9 am to 7 pm depending on the season) being selected about equally.

Health Data The mortality file was obtained from the central Provincial computerized database of death certificates. Death certificates are completed at the time of death either by an attending physician or by the coroner. Identifying information, date of death, place of death, residence at time of death, and the underlying cause of death (coded by government nosologists to the *International Classification of Diseases, Ninth Revision* [ICD-9]) were recorded routinely. Contributing causes of death were not recorded on the file.

Medical services and pharmaceuticals were provided by the QHIP to eligible registrants and the data were recorded as part of routine fee-for-service procedures. The QHIP provides universal coverage to QHIP registrants for all costs of medical and hospital services dispensed in-province and it provides complete or partial coverage for procedures, services, pharmaceuticals, and hospital admissions out-of-province. Thus, almost every person living legally in Quebec during the study period was registered in the plan, including Canadian citizens resident in Quebec, newborns, temporary workers with a valid work permit, and landed immigrants. To have access to medical care, a registrant must produce a valid QHIP card. Inscribed on this card is the QHIP number, which is an unique identifier assigned at registration. This number is recorded on each medical transaction and is used administratively to check the validity of claims.

Addresses of QHIP registrants were recorded by the agency and updates were obtained periodically. In 1987, there was a serious attempt by the QHIP to maintain addresses on a regular basis. Because of uncertainties about the accuracy of these data, we relied on the usual place of address as recorded on the mortality file to identify deceased subjects.

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.

The administrative files of the QHIP include a database of procedures, visits, and consultations carried out by physicians that were submitted for reimbursement. Each record contains the QHIP number, the physician number, the location where the service was rendered (eg, acute care center [hospital, office, emergency room]), date, billing code (eg, type of surgery), specialty of the attending physician, the reason for the visit, and other data relevant to the billing. Prior to 1991, emergency room visits were not identified separately from outpatient clinic visits.

The prescription database contains information from pharmacists on drug prescriptions that were dispensed, including the date that the prescription was filled, name and generic type of medication, quantity, duration of prescription, and authorization for refills. The QHIP paid the costs of prescriptions for persons ≥ 65 years and for those receiving social assistance benefits.

We used hospital discharge data of decedents to verify the record linkage between the mortality file and the QHIP file and to validate our indicators of disease group. (The verification of the record linkage is described below and the validation is presented in Appendix F.) The Quebec Hospital Discharge Registry (MedEcho) is derived from discharge summaries that were reported to a central collection and processing system (Bourdages 1987). Since 1981, all acute care hospitals in Quebec have been required to report to the system; nursing homes and similar types of institutions do not report. Each hospital is responsible for abstracting and verifying its own data. Information on a summary sheet is completed by the treating physicians, retained in the patient's chart, and used by trained nosologists in each hospital to code to the ICD-9 the primary diagnoses that made the largest contribution to length of stay, as well as other comorbid conditions that contributed to length of stay. (A maximum of 15 diagnoses that contributed to the length of stay are recorded on the database.) Personal identifiers, such as names, were not recorded on this file, but QHIP numbers have been included on the database since 1990.

Data Assurance Procedures

For data audit information, see Appendix G.

Identification of the Study Population

We identified subjects from the provincial mortality registry, consisting of all persons who died in Montreal. To identify subjects on the files of the QHIP, we used a nonprobabilistic record linkage procedure. The algorithm (Figure 3) is divided into two segments, according to whether the subject's 12-character QHIP number was present or not on his or her mortality record.* The QHIP number has been recorded on the mortality file only since 1992. If the QHIP number was present, we validated it by ensuring that the last digit, a check digit, was correct. If the QHIP number was not present on the record, a pseudo-QHIP number (10 characters) was created. In both cases, we then carried out a linkage to the set of QHIP numbers on the nominal roll. If the first 10 characters

* The QHIP identifier is a 12-character string unique to each registrant and assigned at birth or at time of registration. The first three characters of the surname take the first three positions; the first initial of the given name is in the fourth position; the birth date (year, month, day) take up the next six positions (50 is added to the month for women); the next character represents a sequence number to distinguish duplicate numbers having the same first 10 characters; and the final character is a check digit.

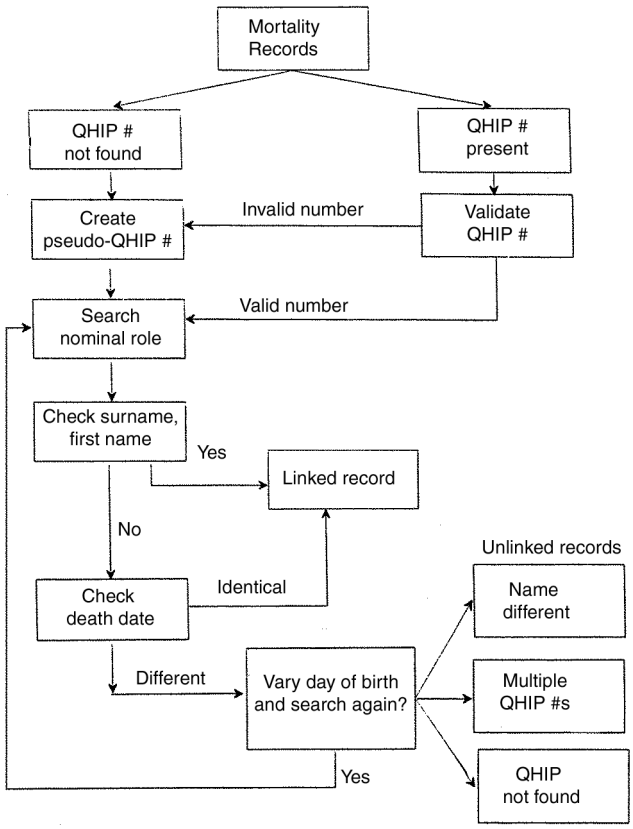

Figure 3. Flow chart for record linkage. The process began by identifying eligible decedents from the mortality register. For subjects whose QHIP number was recorded on the mortality file, we searched the nominal roll of the QHIP. For the remaining subjects, we used first name, surname, date of birth, and gender to generate a pseudo-QHIP number that was then linked to the QHIP's nominal roll. A variety of checks were used to ensure accuracy of the matches. For subjects who could not be linked through these computer algorithms, we attempted a manual record linkage.

were identical, then the link was labeled as a potential match. A definite match was declared if, in addition, the first six characters of the last name and the first three characters of the first name agreed.

For those links with more than one potential match or imperfect agreement on these character strings, we made additional checks on the date of death. If death dates on both records were identical, a definite match was declared. If the date of death was different, then the day of birth was changed by ±1 day and the algorithm was repeated. A manual record linkage was then used to link unmatched subjects. The criteria for declaring a match were equality on name of family, first initial of given name, year of birth, sex, and date of death. However, if no such correspondence was obtained, we replaced this step by permuting the various combinations of family name or given name, or by adding or subtracting one year from the birth year.

We verified accuracy of the QHIP numbers assigned to subjects by comparing hospital discharge records with dates of death. For this purpose, we used the Quebec hospital discharge database for decedents who were hospitalized between 1990 and 1993. We used this restricted time period because, prior to 1990, identifying information (including the QHIP number) was not on the hospital discharge file. Subjects whose files showed a hospital discharge recorded 180 days or more after the reported date of death, or were declared from hospital discharge records to have died prior to the actual date of death, were declared to be false matches and were excluded from the study population.

Lastly, to minimize any biases that may have occurred from migration in or out of the target area, we restricted the statistical analysis to only those persons who were residents of Montreal and who died there during the study period. We had no means of verifying whether potentially eligible subjects were inadvertently excluded from the study population.

Statistical Methods

Correcting Air Pollution Measurements That Were Below the Level of Detection Estimates of statistics of environmental pollutant concentrations should account for measurements below the level of detection; otherwise biases may occur when replacing all values below the level of detection by zero. To correct for this, we developed a Monte Carlo method that is a modification of the triangular method proposed by Hornung and Reed (1990). In order to apply this new method, we first verified that the underlying distribution of each pollutant was normal or log-normal. We then estimated the percentage of values below the level of detection, calculated the slope of the triangle that approximated the censored part of the distribution, and generated a series of random values subject to the constraint that all values fell within the triangle. Using true and simulated data sets, we compared this method with Hornung and Reed's triangular method and with Hald's maximum likelihood approach (Hald 1952; Cohen 1961).

Interpolation of Missing Particle Data Because TSP and PM were not measured daily, we developed statistical models to predict particle and sulfate mass for days when measurements were not taken. The linear regression models incorporated these variables: daily mean COH, corrected extinction coefficient, and levels of sulfate measured daily at the Sutton monitoring station. The justification for using the above variables was that COH is an accurate measure of ambient carbon, Sutton sulfate reflects large-scale background levels of sulfate, and the extinction coefficient

measures, however imperfectly, local concentrations of sulfate. We did not use gaseous pollutants or weather variables to improve the prediction, as we wanted to use these as covariates in the statistical models used to estimate associations between daily mortality and ambient air particles.

We used the following general linear regression prediction model:

$$\mathrm{E}[PART_i] = \alpha + \beta_1\, COH_i + \beta_2\, Extinction_i + \beta_3\, Sutton\ sulfate_i \quad (1)$$

where $\mathrm{E}[PART_i]$ represents expected daily mass concentrations for $PM_{2.5}$ and sulfate from $PM_{2.5}$ (averaged over the two monitoring stations), i is an indicator for the day in the time series, *COH* is the mean daily COH averaged over all monitoring stations in Montreal, *Extinction* is the daily mean extinction coefficient corrected for humidity, and α and β are coefficients that were estimated in each regression model. We used the linear predictor (right-hand side) of equation 1 to estimate concentrations of $PM_{2.5}$ and sulfate from $PM_{2.5}$ for every day in the time series. Because measurements of sulfate at Sutton were available only since 1986, two different models were developed to account for the availability of data: 1984 to 1993 without sulfate at Sutton and 1986 to 1993 with sulfate at Sutton.

Statistical Methods for Estimating the Association Between Daily Cause-Specific Mortality and Ambient Concentrations of Particles

It was assumed that the mortality data were distributed approximately as a Poisson variate with constant over- or underdispersion. Thus, the variance was assumed to be proportional to the expected response, with the scaling parameter representing over- or underdispersion relative to the Poisson model. Overdispersion in the data is related to clustering of deaths in time beyond expected Poisson variability (mean of daily numbers of deaths equal to the variance), and this could arise if the population under study includes subpopulations having different daily death rates (Spix et al 1993). There is no simple and plausible interpretation of underdispersed data. We used quasi-likelihood estimation within the context of the generalized additive models (GAMs) (Hastie and Tibshirani 1990). These flexible regression models allow the estimation of nonparametric smooth functions for potential confounding variables (time, weather variables) and pollutants and allow the estimation of the dispersion parameter. We selected the family of locally weighted regression smoothers (LOESS), as they have enhanced properties at the end points of the time series and facilitate the study of interactions between variables. For each model, the dispersion parameter (ϕ) was estimated and the covariance matrix was then corrected by multiplying the usual Poisson covariance matrix by the estimated dispersion parameter.

As is customary in time-series analyses, we assumed that yearly, seasonal, and subseasonal variations in cause-specific mortality time series represented unmeasured processes (eg, influenza epidemics) that may have confounded the association between mortality and the short-term effects of air pollution. The basic approach was to treat these temporal effects and the climatic variables as nuisance terms in the GAMs. Thus, we regressed the natural logarithm of the daily number of deaths on a LOESS term representing the temporal filter that adjusted for seasonal and subseasonal variations, on another term to account for annual trends in daily mortality, and on LOESS terms to adjust for the potential confounding effects of relevant climatic variables.

We developed statistical models sequentially using the following scheme. For each cause of death considered, we determined which temporal filter removed the seasonal and subseasonal cycles from the data. Because we found a secular increase in mortality, we also added a term for calendar year. Thus, the model was $\mathrm{E}[\log(y_i)] = \alpha +$ LOESS(i,span) + LOESS(year) (y_i is the number of cause-specific deaths on day i) and we selected the optimal span (smoothing bandwidth) that met the following criteria: 1) least amount of residual serial autocorrelation; 2) minimum Akaike Information Criterion (AIC); and 3) consistency of the filtered time series with a white-noise process, as determined from the cumulative periodogram using Bartlett's statistic (Priestly 1981).

The AIC is a penalized version of the deviance, defined as the residual deviance + 2 × dispersion parameter (ϕ) × residual degrees of freedom (df) used in the model. The AIC is appropriate for comparing nonnested models, although no specific statistical test is available. Thus, the model with the lowest value of the AIC is the one that explains the most residual variation, after accounting for the number of degrees of freedom used (Hastie and Tibshirani 1990). Bartlett's statistic is based on the cumulative periodogram, which is a plot of the cumulative amplitude of the Fourier frequencies estimated from the filtered time series; if the cumulative periodogram follows a straight line then each of the Fourier components differs from zero only because of random variation.

The first condition of minimizing residual autocorrelation is extremely important as it is assumed in the quasi-likelihood models that the observations are statistically independent. While in practice not all serial autocorrelation can be removed, small residual correlations will not

greatly affect statistical estimation or inference. In addition, the temporal filtering will remove some of the overdispersion in the mortality time series.

Next, we assumed that weather could confound the association between particles and mortality. It seems clear that extremely high temperatures and humidities are causally related in certain groups and jurisdictions, such as in a 1995 heat epidemic in Chicago, and similarly for cold episodes. We made no assumptions as to whether the effects of weather were concurrent with or preceded each day of death. We searched for the set of weather variables that explained the most residual variation in the data (minimum AIC). The variables were daily mean temperature, daily mean dew point temperature, change in maximum temperature from the previous day, relative humidity, and change in barometric pressure from the previous 24 hours.

Including the temporal filter and the term for year, we developed a series of statistical models for each weather variable separately for lags 0 through 5 days. (The term lag refers to the estimation of effects for exposures that occurred prior to the day of death.) We then examined the AICs for each model, accounting for losses in observations due to the taking of lags, and selected for each variable the lag that produced the minimum AIC. Using these selected variables, we then constructed a series of models that included all combinations of these variables. For each cause of death, we investigated pairwise smooth interactions [LOESS(A_j,B_k), where j and k are lags from 0 to 5], combinations of two individual smooths [LOESS(A_j) + LOESS(B_k)], and combinations of three individual smooths [LOESS(A_j) + LOESS(B_k) + LOESS(C_j)]. The models yielding the minimum AIC were used as the primary weather variables in all subsequent analyses. In addition, we carried out sensitivity analyses using the single weather variable that minimized the AIC.

Single pollutant models using daily mean values across the fixed site monitoring stations were considered first, and lags were obtained by relating mortality with previous days' levels of air pollution. Models using 3-day averages (mean of lags 0 to 2 days; referred to as the *3-day mean*) of air pollutants were also estimated. For those pollutants not measured daily (TSP, PM), we took lags by shifting the mortality time series forward, so that mortality data following the day in which pollutant measurements were taken were regressed against those days in which measurements were made. Multiday averages could not be derived for pollutants that were not monitored daily.

We also carried out cause-specific analyses by age (< 65 and ≥ 65 years) using the same statistical models developed from the full data.

All nontemporal, continuous covariates (weather, pollution) were entered into the model nonparametrically using a LOESS smoother that had a span of 50%. For the particle variables, we used an approximate F test to determine whether the nonlinear component significantly improved the fit over a linear one (Hastie and Tibshirani 1990).

For the parametric, linear modeling of particles, the parameter is interpreted as the relative increase in the logarithmic number of daily deaths per unit increase in the pollutant. The percent change in the mean number of daily deaths was calculated for each index of ambient particles for an increase equal to the interquartile range (IQR): $[\exp(\beta \times \text{IQR}) - 1] \times 100\%$, where β is the estimated regression coefficient. We refer to this quantity as the *mean percent change* (MPC). We obtained the corresponding upper and lower 95% confidence limits on the MPC assuming normality of the regression coefficients, namely $\exp[\text{IQR} \times (\beta \pm 1.96 \times \text{SE}) - 1] \times 100\%$, where SE is the estimated standard error for β (corrected for non-Poisson variability).

Because different spans for the temporal filter may lead to different results, we carried out a series of sensitivity analyses using different spans for the LOESS filter. However, the primary analysis on which we base our conclusions used the spans that satisfied the criteria described above. We also conducted sensitivity analyses using no weather variables as well as using the one weather variable that had the lowest AIC. Additional sensitivity analyses were carried out adjusting for carbon monoxide (CO), nitrogen dioxide (NO_2), nitrogen oxide (NO), O_3, and SO_2. Models that included each of these copollutants separately as well as a model that contained all copollutants were developed.

RESULTS

Study Population

During the period 1984 until 1993, inclusive, 176,943 persons were identified as having died in Montreal (Table 3). After excluding duplicates and subjects who could not be linked, 168,647 death records remained. In addition, after excluding nonresidents of Montreal and ambiguous links, the final study population consisted of 140,939 Montreal residents who died in the city.

In order to estimate a lower bound to the number of subjects linked incorrectly, we applied the error rate found in the comparison with the hospital discharge database (0.20%, calculated as 93/46,300) to the entire study population, leading to an estimate that a total of 283 deaths (95% CI: 225–338 deaths) were linked incorrectly. Given that typical error rates in probabilistic record linkages are on the

Table 3. Results of Record Linkage and Comparison to Quebec Hospital Discharge Records

Parameter	Value
Records	
Records of deaths in Montreal, 1984–1993	176,943
Duplicate records excluded	30
Total Records	176,913
Record Linkage	
Linked records	
Computerized algorithms	165,495
Manual linkage	3,152
Unlinked records	8,266
Total Subjects Linked	168,647
Excluded Subjects	
Not Montreal resident at time of death	27,615
Likely incorrect link: records indicate that subjects stayed in hospital after date of death on death certificate or that date of death on hospital discharge summary preceded date of death on death certificate[a]	93
Total Excluded	27,708
Total Deaths	149,939
Nonaccidental deaths	133,904
Accidental deaths	7,035

[a] Identified from a comparison of 46,300 deceased subjects linked to the Quebec hospital discharge database for 1990–1993.

order of 2% to 5% (Newcombe et al 1983; Wentworth et al 1983; Stampfer et al 1984; Curb et al 1985; Acquavella et al 1986; Shannon et al 1989; Schnatter et al 1990; Goldberg et al 1993), we suspect that the above estimate is understated.

Linkage rates increased with time (Table 4), probably reflecting improvements in the quality of the identifying information in both files. A slightly higher proportion of women were not linked successfully (4.6% versus 3.9% for men), perhaps because of discrepancies in the family name used in the files. (Since about 1975, a woman living in Quebec does not adopt her husband's family name. In older women, however, there can be differences regarding which family name is used in different administrative files.) Single persons had lower rates of record linkage (91.9%) than other persons. Among deceased children under the age of one year, 82.3% were not linked, probably because newborns who died in hospital shortly after birth were never registered with the QHIP. Distributions of key variables for the final study population are shown in Tables A.1 through A.3.

Weather Variables

Table 5 shows the distribution of weather variables used in the analyses. Figures B.7 through B.10 show time-series plots for mean temperature, mean dew point temperature, maximum change in temperature from the previous day, and change in barometric pressure from the previous 24 hours. Dew point temperature and mean temperature should clearly not be used together in any regression model, but the other variables are relatively uncorrelated.

Pollutant Data

Outliers We used graphical patterns to investigate outlying values in the data in neighborhoods around data points above the 95th percentile. In the end, we found no compelling reasons to exclude any of these data points.

Correcting for Missing Values Below Detection Limit

Table 6 shows that adjusting for measurements of COH and the gaseous pollutants below the limit of detection made little difference in either arithmetic or geometric means. As well, the original variances are between 2% and 25% higher than the corrected ones. Corrected mean values are used in all calculations presented below.

Table 4. Characteristics of Linked and Unlinked Subjects Among Deceased Residents of Montreal at Time of Death, 1984 to 1993[a]

Characteristic	Total Deaths	Subjects Linked		Unlinked	
		Computer Link	Manual Link	Subjects	Percentage
Year of Death					
1984	14,117	12,948	349	814	5.8
1985	14,455	13,349	348	756	5.2
1986	14,521	13,424	351	742	5.1
1987	14,837	13,773	392	669	4.5
1988	14,686	13,574	368	740	5.0
1989	15,073	14,071	310	686	4.6
1990	14,661	13,596	348	715	4.9
1991	14,919	14,374	122	421	2.8
1992	14,588	14,148	105	335	2.3
1993	15,421	14,996	86	339	2.2
Sex					
Men	75,755	71,503	1,296	2,941	3.9
Women	71,523	66,750	1,483	3,276	4.6
Age					
≤ 1	1,585	267	13	1,305	82.3
2–9	317	291	6	20	6.3
10–19	604	562	10	32	5.3
20–34	3,788	3,488	102	198	5.2
35–64	32,766	31,081	583	1,097	3.3
65–74	35,586	33,994	563	1,023	2.9
≥ 75	72,632	68,570	1,502	2,542	3.5
Marital Status					
Single	28,211	25,333	576	2,295	8.1
Married	61,806	59,028	970	1,800	2.9
Widowed	47,696	44,827	1,057	1,800	3.8
Divorced	6,531	6,202	107	220	3.4
Separated	3,034	2,863	69	102	3.4
Underlying Cause of Death[b]					
Neoplasms	43,370	41,617	554	1,198	2.8
Digestive	11,668	11,158	190	320	2.7
Lung	11,554	11,181	151	221	1.9
Female breast	3,988	3,808	0	180	4.5
Others	16,160	15,470	213	477	3.0
Cardiovascular diseases	59,446	56,060	1,267	2,103	3.5
Acute coronary artery disease	22,362	21,093	495	770	3.4
Chronic coronary artery disease	13,132	12,475	269	386	2.9
Coronary disease	35,494	33,568	764	1,156	3.3
Cerebrovascular disease	9,835	9,288	198	347	3.5
Others	14,117	13,204	305	600	4.3
Respiratory diseases	11,782	11,178	220	382	3.2
Nonmalignant digestive diseases	5,984	5,719	88	176	2.9

(Table continues next page)

Table 4 ***(continued).*** Characteristics of Linked and Unlinked Subjects Among Deceased Residents of Montreal at Time of Death, 1984 to 1993[a]

Characteristic	Total Deaths	Subjects Linked		Unlinked	
		Computer Link	Manual Link	Subjects	Percentage
Underlying Cause of Death *(continued)*[b]					
Other causes	19,223	16,890	396	1,929	10.0
AIDS	1,516	1,461	13	42	2.8
Diabetes	3,838	3,603	75	158	4.1
Renal diseases	1,852	1,763	36	52	2.8
Neurologic conditions	4,481	4,148	111	221	4.9
Nonaccidental, total	139,805	131,464	2,525	5,790	4.1
Accidents	7,473	6,789	254	427	5.7
All causes, total	147,278	138,253	2,779	6,217	4.2

[a] The table includes 93 subjects who were excluded from information on hospital discharge records. It excludes 15 subjects with duplicate records (30 records total), and thus the column representing the total number of deaths may not equal the sum of columns 3 and 5.

[b] Definitions from *International Classification of Diseases, Ninth Revision* (ICD-9) codes: neoplasms, 140–239; circulatory diseases, 390–459; respiratory, 460–519; and nonmalignant digestive, 520–579. Other causes are represented by all remaining rubrics and include AIDS, 042; diabetes, 250; renal and kidney disease, 580–593; neurological conditions, 013, 036, 046, 269, 290, 294, 310, 320–337, 342, 348–349, 352, 742; digestive cancer, 151–159; lung cancer, 162; breast cancer, 174; acute coronary artery disease, 410–411; chronic coronary artery disease, 412–414; coronary disease, 410–414; cerebrovascular disease, 430–438; and accidents, 800–999.

Table 5. Distribution of Weather Variables, Montreal, 1984 to 1993

Parameter	Units	Mean (SD)	Minimum	Percentile				Interquartile Value
				25th	50th	75th	100th	
Mean temperature	°C	6.4 (11.8)	−27.3	−2.6	7.5	16.5	28.8	19.1
Change in maximum temperature from previous day	°C	0.0 (4.7)	−25.0	−2.5	0.4	2.8	19.4	5.3
Mean dew point temperature	°C	1.2 (11.6)	−33.8	−6.6	2.0	10.8	23.1	17.4
Relative humidity	%	69.4 (11.9)	33.0	61.0	70.0	78.0	99.0	17.0
Change in barometric pressure from previous day	kPa	0.0 (0.9)	−4.2	−0.5	0.0	0.6	4.4	1.1

Table 6. Correcting for Measurements of Coefficient of Haze and Gaseous Pollutants Below Limit of Detection and Comparison with Original Data, Montreal, 1984 to 1993

Pollutant (units)	Mean of Daily Means		Variance of Daily Means		Geometric Means of Daily Means	
	Original	Corrected	Original	Corrected	Original	Corrected
COH[a]	2.44	2.42	2.96	2.37	1.93	1.96
SO_2 (μg/m^3)	16.67	17.78	136.42	126.11	13.55	15.22
O_3 (μg/m^3)	28.56	28.97	300.33	292.41	23.51	24.35
CO (ppm)	0.77	0.80	0.23	0.22	0.65	0.70
NO (μg/m^3)	40.81	41.78	859.66	840.42	32.48	34.02
NO_2 (μg/m^3)	41.42	41.71	243.05	237.78	38.62	39.03

[a] In 0.1 COH units/327.8 linear meters or equivalently in 0.1 COH/1,000 linear feet.

Temporal and Spatial Variation in Levels of Environmental Pollutants We found considerable temporal variation in mean daily levels of pollutants (see Appendix B for scatterplots). Seasonal and subseasonal cycles account for much of the variability (Table C.8), although the scatterplots show that secular changes were also important. With the exception of O_3, extinction coefficient, and sulfate from PM, mean levels of pollutants decreased dramatically during the study period (Table 7). Particulate matter, COH, extinction, and gaseous pollutants (except O_3) had peaks in the winter (Appendix B). For sulfate and O_3, as expected, we found peaks in the summer months. We also found that TSP was elevated in both winter and spring; the spring elevations can be explained by the extensive use of salt and gravel on roadways during the winters that remain until late spring.

Considerable spatial variation of daily mean values was imposed on this seasonal and subseasonal variability (Table 7). In particular, higher mean levels of TSP and COH were found at monitoring stations located near two limestone quarries (one now serves as a municipal solid waste landfill site while the other is inactive) that are both located along a major east-west highway through the city (Figure 4, Montreal monitor map). (Mean values for levels of pollutants for all of the monitoring stations are shown in Appendix C.) Despite these elevated values, correlation coefficients averaged over all pairs of monitoring stations were similar to those averaged over the subset excluding these four stations.

We attempted to confirm that mean daily concentrations averaged across all monitoring sites were an appropriate exposure metric for TSP and PM. Therefore, we conducted a small pilot study of spatial variation of levels of TSP and PM_{10} around the fixed monitoring stations (Appendix C). For TSP, we found that levels in residential areas can be represented by fixed monitoring stations located in other residential neighborhoods within 6 km and that levels observed in areas with heavy traffic are significantly higher than those observed at 1 or 3 km distance. For PM_{10}, the spatial distribution was much more homogenous and the monitoring station located downtown was representative of levels as far off as 14 km from the site (Brook et al 1997b).

Table 7. Correlations and Trends in Measured Environmental Pollutants, Montreal, 1984 to 1993

Pollutant (units)	Number of Monitoring Stations	Range of Mean Values Between Stations, 1984–1993	Coefficient of Variation of Daily Means, 1984–1993 (%)	Range of Pearson Correlation Coefficients Between Monitoring Stations	Means of Daily Means Across Study Years		
					Mean 1984–1985	Mean 1992–1993	Average Annual Change[a]
TSP ($\mu g/m^3$)	19	32.9–88.3	42.6	0.2–0.9	59.4	44.4	–2.08
PM_{10} ($\mu g/m^3$)	2	27.8–44.5	54.7	0.7	40.0	26.4	–1.98
$PM_{2.5}$ ($\mu g/m^3$)	2	16.2–21.1	65.3	0.9	20.2	14.9	–0.87
Sulfate from TSP ($\mu g/m^3$)	13	2.3–6.0	68.7	0.3–1.0	5.2	3.6	–0.21
Sulfate from PM_{10} ($\mu g/m^3$)	2	4.6	92.0	0.9	4.9	4.5	–0.08
Sulfate from $PM_{2.5}$ ($\mu g/m^3$)	2	4.0–4.2	97.7	0.9	4.3	4.1	–0.06
Total sulfate from Sutton monitoring station[b] ($\mu g/m^3$)	1	3.35	107.5	—	2.83[c]	2.9	–0.03
COH[d]	11	1.2–4.2	63.9	0.2–0.7	2.6	1.9	–0.10
Extinction (corrected)	1	0.15	66.7	—	0.15	0.15	0.00
SO_2 ($\mu g/m^3$)	13	11.1–30.7	63.2	0.1–0.8	22.6	14.0	–0.96
NO_2 ($\mu g/m^3$)	8	30.3–61.9	37.0	0.2–0.6	44.9	40.2	–0.45
NO ($\mu g/m^3$)	8	20.2–89.9	69.4	0.3–0.8	51.0	36.4	–1.73
CO (ppm)	12	0.5–5.8	58.8	0.1–0.8	1.1	0.6	–0.77
O_3 ($\mu g/m^3$)	9	16.6–43.1	59.0	0.5–0.9	29.3	28.9	0.08

[a] Calculated from a linear regression model.

[b] For the period 1986 to 1993.

[c] For 1986.

[d] 0.1 COH units/327.8 linear meters.

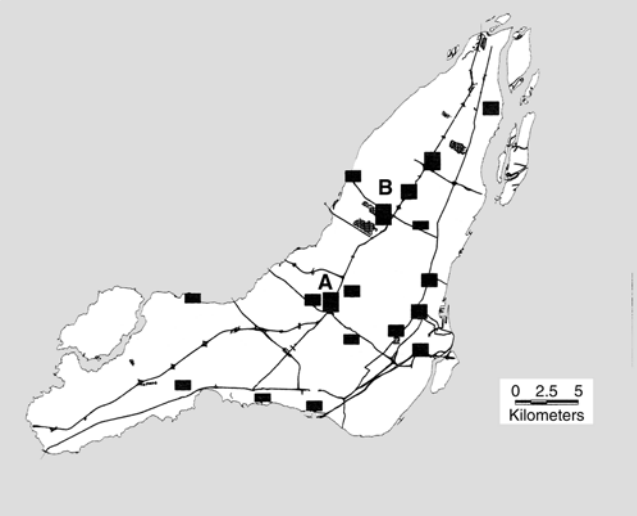

Figure 4. Montreal map showing TSP monitoring sites. The dark lines indicate major expressways. One monitoring station with high levels of pollutants is at the junction of two major highways (A), and a second is at the site of two former limestone quarries (B).

We found that the distribution of sulfate over long distances was fairly homogeneous, as shown by the high Pearson correlation coefficients (~0.9) between measurements of total sulfate at the Sutton monitoring station (about 150 km southeast of the city) and mean values of sulfate from PM at the two NAPS monitoring stations in Montreal (Table C.4). The correlations for sulfate were still reasonably high when measurements were lagged by one day, but decreased considerably for lags of two days or more.

Prediction of Missing Particle Data Daily measurements of total sulfate made at the Sutton acid rain monitoring station, daily mean values of COH, and the daily estimated value of the extinction coefficient were used to assemble a synthetic time series for $PM_{2.5}$ and sulfate from $PM_{2.5}$. The Pearson correlation coefficients between the three predictor variables ranged from 0.27 to 0.49. The predictions of $PM_{2.5}$ and sulfate derived from $PM_{2.5}$ were fairly accurate ($R^2 = 0.72$ and $R^2 = 0.80$, respectively). The two predicted time series were thus derived from the linear predictor of the fitted models for all time points.

Table 8. Distribution of Mean Daily Environmental Pollutants Averaged over All Monitoring Stations, Montreal, 1984 to 1993

Pollutant (units)	Number of Monitoring Stations[a]	Number of Days of Measurements[a]	Mean (SD)	Minimum	25th	50th	75th	100th	Interquartile Value
TSP ($\mu g/m^3$)	19	603	53.1 (22.6)	14.6	37.0	48.7	65.6	211.1	28.57
PM_{10} ($\mu g/m^3$)	2	624	32.2 (7.6)	6.5	19.7	28.5	41.1	120.5	21.32
$PM_{2.5}$ ($\mu g/m^3$)	2	636	17.4 (11.4)	2.2	9.4	14.7	21.9	72.0	12.51
Sulfate from PM_{10} ($\mu g/m^3$)	2	437	4.7 (4.4)	0.3	1.9	3.6	5.7	30.7	3.84
Sulfate from $PM_{2.5}$ ($\mu g/m^3$)	2	446	4.3 (4.2)	0.2	1.6	3.1	5.1	29.2	3.51
Sulfate from TSP ($\mu g/m^3$)	13	607	4.3 (2.9)	0.3	2.3	3.6	5.3	19.2	3.02
Total sulfate from the Sutton monitoring station[b] ($\mu g/m^3$)	1	2,680	3.3 (3.6)	0	1.3	2.2	3.8	30.0	2.50
COH[c]	11	3,653	2.4 (1.5)	0.1	1.3	2.1	3.2	15.6	1.85
Extinction (corrected)	1	3,454	0.15 (0.10)	0.01	0.06	0.15	0.17	1.87	0.11
Predicted $PM_{2.5}$ ($\mu g/m^3$)	N/A	N/A	17.6 (8.8)	4.6	11.5	15.4	21.0	71.7	9.50
Predicted sulfate from $PM_{2.5}$ ($\mu g/m^3$)	N/A	N/A	4.1 (3.6)	0.02	1.9	3.1	4.8	30.1	2.90
SO_2 ($\mu g/m^3$)	13	3,653	17.8 (11.2)	3.9	10.3	14.6	21.8	105.7	11.50
NO_2 ($\mu g/m^3$)	8	3,653	41.7 (15.4)	8.8	30.9	39.5	50.2	143.5	19.34
NO ($\mu g/m^3$)	8	3,653	41.8 (29.0)	2.7	21.9	34.8	52.3	281.4	30.41
CO (ppm)	12	3,653	0.8 (0.5)	0.1	0.5	0.7	1.0	5.1	0.50
O_3 ($\mu g/m^3$)	9	3,653	29.0 (17.1)	2.8	16.6	26.0	37.9	163.9	21.34

[a] N/A = not applicable.

[b] For the period 1986 to 1993.

[c] 0.1 COH units/327.8 linear meters.

Distribution of Variables Table 8 shows the distributions of measured and predicted pollutants. Mean levels of pollutants in Montreal were lower than have been reported in most American cities. As one would expect, mean values of the measured and predicted indices were similar but variances (and therefore interquartile values) were smaller for the predicted time series. This last finding is a direct consequence of predicting missing data using multiple linear regression.

Strong positive correlations were observed between COH and $PM_{2.5}$ and all of the gaseous pollutants except O_3 (Tables C.4 and C.5). The negative correlations with O_3 and all measures of particles except sulfate resulted from higher values of sulfate and O_3 in the summer. Little correlation was found between total sulfate measured at the Sutton station and the gaseous pollutants, except for O_3 for which a fairly strong correlation ($r = 0.44$) was observed (also due to the summer peaks). Correlations for predicted $PM_{2.5}$ were similar to the original $PM_{2.5}$ time series.

COH was relatively uncorrelated with sulfate but correlated well with fine particles, the extinction coefficient correlated well with fine particles and sulfate, and excellent correlation was found between Sutton sulfate, sulfate measured in Montreal, and the extinction coefficient (Appendix C). Except for O_3, we found that the gaseous variables were positively correlated (Table C.4). We found no correlation between O_3 and NO_2, and strong negative correlations between O_3 and NO ($r = -0.47$) and CO ($r = -0.33$).

Summary In summary, we had fairly complete particle data for the extinction coefficient, COH, and total sulfate measured at the Sutton station (see Appendices B and C, and Table 8). To provide reasonably robust estimates of daily mortality associated with fine particles, we developed a multiple regression model to predict $PM_{2.5}$ and sulfate from $PM_{2.5}$ for days in which we did not take measurements. As statistical power would be greatly reduced for pollutants with incomplete data, we relied on data that were measured daily (COH, extinction, sulfate from Sutton). Although COH is not frequently used in health studies, it is a reliable measure of ambient carbon (mostly from sources of internal combustion; see Table 9) although it does not adequately measure sulfate (they do not add substantially to the opacity of the filter paper). On the other hand, the extinction coefficient is a reasonably good measure of fine particles (Özkaynak et al 1985) and sulfate (Pearson correlation coefficient with sulfate from $PM_{2.5}$ of 0.62), as these particles contribute appreciably to the absorption and scattering of light. It may, however, be more error-prone than other PM measures because it is based on subjective estimates of distance.

Association Between Cause-Specific Mortality and Measures of Ambient Particle Air Pollution

Table 10 shows the distribution of the daily number of deaths by cause and by age group (see Figures B.11 through B.19 for the time-series plots of cause-specific mortality). Mortality was overdispersed (variance greater than the mean) by varying amounts (0% to 44%), and none

Table 9. Correlation Matrix Comparing Coefficient of Haze, Elemental and Organic Carbon, and Particle Mass Analyzed from Monitors Located Near Each Other in Ontario[a]

Pollutant	COH	Fine Elemental Carbon	Coarse Elemental Carbon	PM_{10} Elemental Carbon	Fine Elemental and Organic Carbon
All Measurements					
Fine elemental carbon	0.67	1.00			
Coarse elemental carbon	0.72	0.70	1.00		
PM_{10} elemental carbon	0.71	0.99	0.77	1.00	
Fine elemental and organic carbon	0.69	0.89	0.70	0.90	1.00
$PM_{2.5}$	0.45	0.34	0.21	0.34	0.53
Summer Measurements					
Fine elemental carbon	0.97	1.00			
Coarse elemental carbon	0.85	0.87	1.00		
PM_{10} elemental carbon	0.97	1.00	0.89	1.00	
Fine elemental and organic carbon	0.95	0.96	0.84	0.96	1.00
$PM_{2.5}$	0.61	0.62	0.75	0.64	0.74

[a] Unpublished data courtesy of Dr Jeffrey R Brook, Environment Canada, Toronto, Ontario. Based on measurements taken in South Etobicoke, Ontario, in March–April and July 1998.

Table 10. Daily Mortality in Montreal, 1984 to 1993, by Cause of Death and Age Group

Underlying Cause of Death	ICD-9 Code	Total Number of Deaths	Number of Days with No Deaths	Mean	Variance	Variance/ Mean	Percentile			
							25th	50th	75th	100th
All Causes	1–999	140,939	0	38.6	52.9	1.37	33	38	43	91
< 65 years		36,359	1	10.0	10.5	1.05	8	10	12	26
≥ 65 years		104,580	0	28.6	40.8	1.43	24	28	33	80
Nonaccidental	1–799	133,904	0	36.7	51.5	1.40	32	36	41	89
< 65 years		31,756	3	8.7	9.1	1.05	7	8	11	22
≥ 65 years		102,148	0	28.0	40.2	1.44	24	28	32	79
Neoplasms	140–239	42,140	0	11.5	12.0	1.04	9	11	14	25
< 65 years		14,023	84	3.8	3.8	1.00	2	4	5	12
≥ 65 years		28,117	0	7.7	8.4	1.09	6	8	9	22
Lung cancer	162	11,322	174	3.1	3.2	1.03	2	3	4	12
< 65 years		4,261	1,113	1.2	1.2	1.00	0	1	2	6
≥ 65 years		7,061	543	1.9	2.0	1.05	1	2	3	9
Cardiovascular Diseases	390–459	57,296	0	15.7	19.3	1.23	13	15	18	42
< 65 years		9,644	289	2.6	2.8	1.08	1	2	4	11
≥ 65 years		47,652	0	13.0	15.7	1.21	10	13	16	40
Coronary Artery Disease	410–414	34,313	0	9.4	10.8	1.15	7	9	12	23
< 65 years		6,414	671	1.8	1.8	1.00	1	2	3	8
≥ 65 years		27,899	0	7.6	8.5	1.12	5	7	10	19
Respiratory Diseases	460–519	11,394	216	3.1	3.8	1.23	2	3	4	12
< 65 years		1,428	2,468	0.4	0.4	1.00	0	0	1	4
≥ 65 years		9,966	321	2.7	3.3	1.22	1	2	4	11
Nonmalignant Digestive Diseases	520–579	5,802	740	1.6	1.6	1.00	1	1	2	8
< 65 years		1,708	2,273	0.5	0.5	1.00	0	0	1	5
≥ 65 years		4,094	1,195	1.1	1.1	1.00	0	1	2	8
Other Nonaccidental Causes	580–799	17,272	49	4.7	5.7	1.21	3	5	6	16
< 65 years		4,953	1,025	1.4	1.5	1.07	0	1	2	7
≥ 65 years		12,319	156	3.4	3.9	1.15	2	3	5	14
AIDS	042	1,472	2,561	0.4	0.5	1.25	0	0	1	5
< 65 years		1,453	2,570	0.4	0.5	1.25	0	0	1	5
≥ 65 years		19	3,634	0.0	0.0	—	0	0	0	1
Diabetes	250	3,677	1,361	1.0	1.1	1.10	0	1	2	7
< 65 years		730	2,987	0.2	0.2	1.00	0	0	0	4
≥ 65 years		2,947	1,655	0.8	0.8	1.00	0	1	1	5
Renal Diseases	580–593	1,798	2,224	0.5	0.5	1.00	0	0	1	6
< 65 years		233	3,425	0.1	0.1	1.00	0	0	0	2
≥ 65 years		1,565	2,365	0.4	0.4	1.00	0	0	1	6
Neurological conditions[a]		4,256	1,188	1.2	1.3	1.08	0	1	2	7
< 65 years		472	3,214	0.1	0.1	1.00	0	0	0	2
≥ 65		3,784	1,361	1.0	1.2	1.20	0	1	2	7
Accidents	800–999	7,035	567	1.9	2.1	1.11	1	2	3	9
< 65 years		4,603	1,083	1.3	1.4	1.08	0	1	2	9
≥ 65 years		2,432	1,891	0.7	0.7	1.00	0	0	1	7

[a] IDC-9 codes: 013, 036, 046, 269, 290, 294, 310, 320–337, 342, 348, 349, 352, 742.

of the time series was underdispersed. The daily mean number of nonaccidental deaths was 36.7 with the main contributions being from cardiovascular (mean of 15.7), neoplastic (11.5), and respiratory (3.1) deaths. On three days (September 4, 1984, with 14 deaths; August 8 and 9, 1986, with 21 deaths), the number of deaths was particularly low. For September 4, we observed considerable variation in the number of deaths in the vicinity of this day (29, 41, 14, 30, 31) but not as much variation for August 8 and 9 (32, 37, 21, 21, 32, 38).

The first step in the statistical analysis was to find, for each cause of death, a set of temporal filters that minimized the serial autocorrelation, minimized the residual variation (AIC), and produced a time series of residuals that were relatively compatible with what would be expected from a pure white noise process. As an illustration of the method, all nonaccidental causes of death had substantial serial autocorrelation (~0.25 for 1-day lag). The temporal filter with a span of 91/3,653 days (2.49% of the data used for the smoothing) had the lowest AIC (4,131.7; Tables D.1 and D.2), the lowest value for the Bartlett test for white noise, and it virtually eliminated the serial autocorrelation (Appendix D). Although the Bartlett statistic was statistically significant ($p = 0.036$), thus suggesting that the process was not entirely consistent with a random process, other filters led to even smaller p values. (Significance is easily achieved here because of the large numbers of observations.)

No one temporal filter fitted all of the mortality endpoints. Because some days had missing data for most estimates of particles (except for COH), most analyses entailed the use of a partial time series of deaths, and it is possible that the temporal filter did not meet the above criteria with these particular data sets.

Table 11. Association of Nonaccidental Mortality with Coefficient of Haze Evaluated at 3-Day Mean Using a Temporal Filter with a Span of 2.49% of Total Time Series (3,653 Days), Montreal, 1984 to 1993

Model	Terms[a]	AIC	Residual Deviance	ϕ[b]	β for COH	Corrected Standard Error	Corrected *t* Statistic
Temporal Models							
M_1	Lo(time, span = 2.49%)	4126.1	3960.9	1.11			
M_2	M_1 + Lo(Year)	4131.2	3957.5	1.11			
Multiple Weather Variable Models							
M_3	M_2 + Lo(Mean Temperature$_0$, Change in Pressure$_0$)	4046.0	3856.4	1.08			
M_4	M_3 + Lo(COH)	4043.4	3844.5	1.08			
M_5	M_3 + COH	4046.4	3854.5	1.08	0.01060	0.00247	4.290
Single Copollutant Variable Models							
M_6	M_5 + Lo(SO_2)	4045.7	3844.1	1.08	0.00828	0.00273	3.033
M_7	M_5 + Lo(CO)	4050.2	3848.2	1.08	0.00838	0.00287	2.917
M_8	M_5 + Lo(NO_2)	4047.6	3846.1	1.08	0.00842	0.00277	3.044
M_9	M_5 + Lo(O_3)	4053.0	3851.4	1.08	0.01054	0.00252	4.202
M_{10}	M_5 + Lo(NO)	4045.8	3844.4	1.08	0.00926	0.00274	3.381
Multiple Copollutant Variable Models							
M_{11}	M_5 + Lo(SO_2) + Lo(CO) + Lo(NO_2) + Lo(O_3) + Lo(NO)	4069.1	3827.8	1.08	0.00824	0.00299	2.757
None and Single Weather Variables							
M_{12}	M_2 + COH	4119.3	3943.9	1.11	0.01069	0.00244	4.380
M_{13}	M_2 + Lo(Mean Temperature$_0$) + COH	4064.9	3884.9	1.09	0.01082	0.00245	4.415

[a] Weather variables evaluated on the concurrent day. Lo(Mean Temperature$_0$, Change in Pressure$_0$) refers to the smooth interaction of these variables. Lo refers to the LOESS smoother (span of 50%). M = model.

[b] Estimate of dispersion parameter.

The next step was to select the weather variables to be included in the model. After incorporating temporal effects, the single term that explained the most variation in the mortality series was the LOESS function (using a span of 50% of the data) of mean temperature evaluated on the day of death [LOESS(Mean temperature$_0$); AIC = 4,064.0]. After considering multiple variables, the combination that explained the most variation was a LOESS interaction between mean temperature and change in barometric pressure from the previous day, both evaluated at lag 0 (AIC = 4,045.3). Different sets of weather terms were used in the analyses of the other cause-specific time series (Appendix D).

Table 11 shows the modeling strategy for an important measure of particles, COH (evaluated at the 3-day mean). The first step was to filter temporal trends in the data (model M_1). The baseline model (M_2) included the temporal filter and a LOESS term for calendar year. This temporal filtering reduced the overdispersion from 40% found in the crude mortality series to 11%. Adding in the weather variables reduced the overdispersion to 8% and decreased the AIC by 85.2. The exposure-response curve for COH was determined also by using LOESS (using a span of 50% of the data). Adding this term to the model (model M_4) reduced the AIC by 2.1 and did not alter the amount of overdispersion. The likelihood ratio test for including this term was highly significant (χ^2 = 11.9 on 6.5 *df*), suggesting that the LOESS function for COH significantly improved the fit. The graph of the fitted LOESS function for COH showed some nonlinearity, and this was reflected in the fact that the AIC was higher than that obtained in the nonparametric fit (Figure 5). The simple linear parametric form showed a statistically significant slope (corrected t = 4.290). (For lag 0, we found that the exposure-response function was consistent with a linear effect.)

From this last model (M_5), the MPC in the number of daily deaths for an increase in the 3-day mean of COH across its IQR (1.85) was 1.98% (95% CI: 1.07%–2.90%). We found some variation in the results after adjusting for single gaseous pollutants (SO_2, CO, NO_2, NO, O_3; models M_6 to M_{10}, all evaluated at lag 0) and all pollutants combined (model M_{11}), with a slight attenuation in effects observed for all models (all t values were greater than 2). Similar results were found when no and one weather variables were included in models M_{12} and M_{13}, respectively.

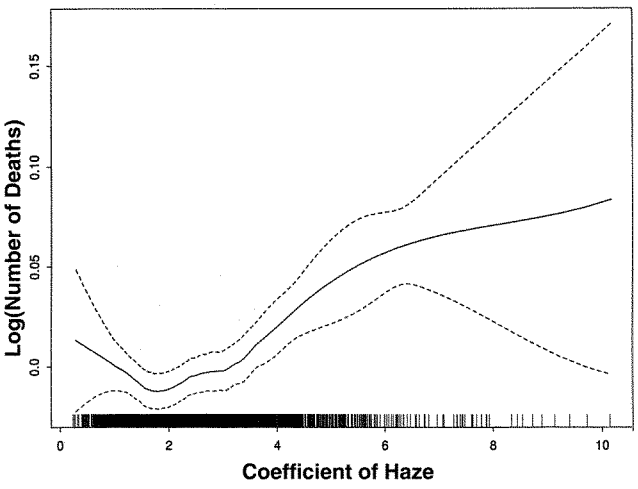

Figure 5. The fitted LOESS line (solid line) and 95% pointwise confidence limits (broken lines) showing association between daily nonaccidental mortality and coefficient of haze at the 3-day mean. The statistical model includes the temporal filter (2.49%), a term for calendar year, and the LOESS interaction term (50% span) between mean temperature (°C) and change in barometric pressure (kPa) from the previous day, all evaluated at lag 0. The ordinate represents the expected logarithmic number of daily nonaccidental deaths, and the abscissa represents the coefficient of haze. The solid line is the LOESS smooth representing the long-term trend (50% span). The rug plot at the bottom of the figure represents data points in the time series. Daily counts of mortality, on the natural logarithmic scale, between any two values of the coefficient of haze can be read directly from the ordinate, and relative changes between these two points can be calculated by taking the exponential of the difference between these two values.

Results by Particle Measure

We conducted separate analyses for each cause of death listed in Table 10 for all the particle pollutants for which there were available data. We analyzed each pollutant on the day of death (lag 0), the preceding day (lag 1), and the mean of exposures across the concurrent day and the two preceding days (referred to as the 3-day mean), by cause of death and by age group. For the purposes of this report, we present results for three pollutants evaluated for the 3-day mean: COH, predicted $PM_{2.5}$, and sulfate measured at the Sutton station. (Detailed results for all causes of death, for all pollutants, all three lag periods, and age groups are given in Appendices H through O, which are available on request from the Health Effects Instutute and on the HEI web site.) The analyses in these tables did not take into account the effects of gaseous pollutants (Table 12). The appendices also include figures that provide results by cause of death for all indices of particle air pollution by lag and age group.

Table 13 shows the MPC in daily mortality for an increase in level of exposure of the above-mentioned three pollutants, evaluated at the 3-day mean across each pollutant's IQR. Across all ages, we found consistent elevations in daily mortality across these three measures of particles for deaths from all nonaccidental causes, respiratory diseases, other nonaccidental causes, and diabetes. For COH, we also observed statistically significant increases for neoplasms and lung cancer; for total sulfate

Table 12. Sensitivity Analyses: Effect of Different Gaseous Pollutants on Estimates of Excess Relative Risk for Nonaccidental Causes of Death Across Interquartile Range of COH, Predicted $PM_{2.5}$, and Sutton Sulfate at 3-Day Mean, Montreal, 1984 to 1993

Pollutant and Cause of Death	Primary Analysis (M_1)[a]	$M_2 = M_1 + Lo(SO_2)$	$M_3 = M_1 + Lo(CO)$	$M_4 = M_1 + Lo(NO_2)$	$M_5 = M_1 + Lo(NO)$	$M_6 = M_1 + Lo(O_3)$	$M_7 = M_1 + Lo(SO_2) + Lo(CO) + Lo(NO_2) + Lo(NO) + Lo(O_3)$
Coefficient of Haze							
Nonaccidental deaths	1.98[b]	1.54[b]	1.56[b]	1.57[b]	1.73[b]	1.98[b]	1.54[b]
Neoplasms	2.34[b]	1.95[b]	2.27[b]	2.32[b]	2.76[b]	2.79[b]	2.41[b]
Cardiovascular diseases	0.19	−0.15	0.08	−0.15	−0.27	0.25	−0.06
Coronary artery disease	0.94	0.30	1.18	0.54	0.46	1.15	0.74
Respiratory diseases	5.98[b]	5.47[b]	4.61[b]	5.00[b]	6.25[b]	4.80[b]	4.12[b]
Digestive diseases	−1.28	−1.57	−2.64	−3.32	−1.92	−1.32	−3.26
Other nonaccidental causes	5.14[b]	4.16[b]	4.26[b]	5.11[b]	5.62[b]	4.74[b]	4.24[b]
Accidents	3.52	4.80[b]	4.12	3.89	3.94	4.40[b]	5.43[b]
Predicted $PM_{2.5}$							
Nonaccidental deaths	2.17[b]	2.20[b]	1.92[b]	2.11[b]	2.12[b]	2.02[b]	1.93[b]
Neoplasms	1.40	1.22	1.10	1.43	1.48	1.28	0.90
Cardiovascular diseases	1.31	1.49[b]	1.50[b]	1.39	1.41	1.39[b]	1.51
Coronary artery disease	1.68	1.93	2.13[b]	1.79	1.72	1.61	2.00
Respiratory diseases	7.73[b]	8.11[b]	7.32[b]	8.08[b]	7.67[b]	6.31[b]	7.01[b]
Digestive diseases	1.90	1.41	1.20	−0.03	1.77	1.22	−0.57
Other nonaccidental causes	3.93[b]	3.40[b]	2.82[b]	3.63[b]	3.51[b]	3.50[b]	2.80[b]
Accidents	2.34	2.96	3.11	2.66	3.00	2.60	3.41
Sutton Sulfate							
Nonaccidental deaths	1.29[b]	1.37[b]	1.32[b]	1.36[b]	1.37[b]	1.13[b]	1.25[b]
Neoplasms	0.75	0.76	0.71	0.87	0.72	0.50	0.47
Cardiovascular diseases	1.31[b]	1.34[b]	1.37[b]	1.33[b]	1.36[b]	1.15[b]	1.33[b]
Coronary artery disease	1.50[b]	1.58[b]	1.57[b]	1.50[b]	1.43[b]	1.12	1.37[b]
Respiratory diseases	3.86[b]	3.74[b]	3.81[b]	3.85[b]	3.96[b]	3.29[b]	3.48[b]
Digestive diseases	0.67	0.40	0.57	0.01	0.86	−0.40	−0.84
Other nonaccidental causes	2.04[b]	1.85[b]	1.92[b]	1.85[b]	2.14[b]	1.88[b]	1.69
Accidents	2.00	2.06	1.97	1.99	2.27	2.23	2.21

[a] M = model.

[b] A corrected t value > 1.96.

Table 13. Summary Estimates of Mean Percent Change in Daily Mortality Across the Interquartile Ranges of Three Selected Measures of Particulate Matter Air Pollution, Evaluated at 3-Day Mean, Montreal, 1984 to 1993[a]

	Coefficient of Haze		Predicted $PM_{2.5}$		Sutton Sulfate	
Cause of Death	Mean % Change[b]	95% CI	Mean % Change[b]	95% CI	Mean % Change[b]	95% CI
Nonaccidental Deaths	1.98	1.07, 2.90	2.17	1.26, 3.08	1.29	0.68, 1.90
Neoplasms	2.34	0.77, 3.93	1.40	–0.14, 2.96	0.75	–0.28, 1.78
Lung cancer	3.05	0.04, 6.15	1.82	–1.13, 4.85	0.39	–1.60, 2.41
Cardiovascular Diseases	0.19	–1.15, 1.54	1.31	–0.06, 2.70	1.31	0.37, 2.26
Coronary artery disease	0.94	–0.80, 2.72	1.68	–0.12, 3.51	1.50	0.28, 2.74
Respiratory Diseases	5.98	3.01, 9.03	7.73	4.74, 10.81	3.86	1.81, 5.95
≥ 65 years	6.90	3.69, 10.21	9.03	5.83, 12.33	4.64	2.46, 6.86
Nonmalignent Digestive Diseases	–1.28	–5.40, 3.02	1.90	–2.19, 6.15	0.67	–2.12, 3.54
Other Nonaccidental Causes	5.14	2.62, 7.71	3.93	1.51, 6.40	2.04	0.41, 3.69
AIDS	7.43	–0.29, 15.75	3.40	–3.41, 10.69	0.51	–4.06, 5.30
Diabetes	7.50	1.96, 13.34	7.59	2.36, 13.09	4.48	1.08, 7.99
Renal diseases	0.25	–6.65, 7.66	–1.66	–8.39, 5.56	–0.10	–4.62, 4.63
Neurologic conditions	1.98	–3.01, 7.23	0.66	–3.78, 5.30	0.12	–2.84, 3.17
Accidents	3.38	–0.45, 7.37	2.04	–1.77, 6.00	1.73	–0.68, 4.20

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=x) + \text{LOESS}(\text{year}) + \text{multiple weather variables} + \beta\,(\text{pollutant})$, where i is an indicator for day and x is the selected span (percent) (Appendix D). Sulfate data from the Sutton monitoring station were available only for 1986 to 1993. See Appendix D for the included weather variables.

[b] Mean percent change calculated for an increase of exposure equal to the interquartile value (Table 8).

Table 14. Mean Percent Change in Daily Mortality Across the Interquartile Ranges for Three Selected Measures of Particulate Air Pollution, Evaluated at 3-Day Mean by Age Group, Montreal, 1984 to 1993[a]

	< 65 Years		≥ 65 Years	
Pollutant and Cause of Death	MPC[b]	95% CI	MPC[b]	95% CI
Coefficient of Haze				
Nonaccidental deaths	0.30	−1.45, 2.09	2.57	1.51, 3.63
Neoplasms	0.33	−2.28, 3.01	3.28	1.31, 5.29
Lung cancer	5.22	0.37, 10.30	1.74	−2.08, 5.71
Cardiovascular diseases	−2.08	−5.12, 1.06	0.76	−0.71, 2.26
Coronary artery disease	−3.92	−7.62, −0.06	2.03	0.09, 4.00
Other nonaccidental causes	4.25	−0.42, 9.14	5.35	2.39, 8.40
Predicted $PM_{2.5}$				
Nonaccidental deaths	1.03	−0.74, 2.83	2.68	1.65, 3.73
Neoplasms	0.51	−2.05, 3.13	1.80	−0.08, 3.72
Lung cancer	0.50	−4.13, 5.36	2.59	−1.19, 6.52
Cardiovascular diseases	0.54	−2.72, 3.91	1.41	−0.07, 2.92
Coronary artery disease	1.50	−2.62, 5.80	1.74	−0.22, 3.73
Other nonaccidental causes	3.98	−0.39, 8.54	3.84	1.02, 6.75
Sutton Sulfate				
Nonaccidental deaths	0.04	−1.16, 1.25	1.77	1.08, 2.48
Neoplasms	−0.36	−2.08, 1.40	1.32	0.05, 2.60
Lung cancer	−3.19	−6.33, 0.05	2.51	−0.03, 5.12
Cardiovascular diseases	0.59	−1.68, 2.90	1.43	0.41, 2.46
Coronary artery disease	1.93	−0.90, 4.85	1.42	0.09, 2.77
Other nonaccidental causes	1.77	−1.16, 4.78	2.15	0.22, 4.11

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=x) + \text{LOESS}(\text{year}) + \text{multiple weather variables} + \beta\ (\text{pollutant})$, where i is an indicator for day and x is the selected span (percent) (Appendix D). Sulfate data from the Sutton monitoring station were available only for 1986 to 1993. See Appendix D for the included weather variables.

[b] Mean percent change calculated for an increase of exposure equal to the interquartile value (Table 8).

from the Sutton station, we found elevated daily mortality for cardiovascular diseases and coronary artery diseases. Estimates at the 3-day mean were generally higher than those at lags 0 and 1 days (Appendix E). These associations were generally stronger among persons ≥ 65 years than for those under age 65 (Table 14), although the 95% CIs for the two age groups overlapped. Among persons ≥ 65 years, we found higher MPCs in the analyses of all three pollutants for all nonaccidental deaths, neoplasms, and for other nonaccidental deaths. In the elderly, we found for predicted $PM_{2.5}$, higher MPCs for lung cancer and cardiovascular disease, and for Sutton sulfate, higher MPCs for cardiovascular disease.

In the analyses described above, it was assumed that a parametric linear term could be used to adequately represent the pattern of exposure to particles and daily mortality. Using the approximate partial F test associated with the LOESS function for particles, we assessed whether there were any important nonlinearities in the estimated exposure-response functions. Most of the data are explained by simple linear parametric models, although significant nonlinearity was observed in the fitted observed LOESS functions for some associations. For these, we perused the LOESS plots to determine whether deviations from linearity were important in terms of our changing our conclusions regarding the strength and direction of the association. Of the 31 associations showing statistically significant nonlinearity, we found four associations that may lead to slightly different interpretations of the data: J-shaped relationships between all nonaccidental causes of death and COH and predicted $PM_{2.5}$ evaluated at the 3-day mean, and between all other

Table 15. Synthesis of Results of Mean Percent Change in Daily Mortality from Different Measures of Particulates Evaluated at the 3-Day Mean Across the Interquartile Ranges of the Various Pollutants, Montreal, 1984 to 1993[a]

Cause of Death	COH	Extinction	Predicted $PM_{2.5}$	Sutton Sulfate	Predicted Sulfate from $PM_{2.5}$
Nonaccidental Deaths	1.98[b]	1.67[b]	2.17[b]	1.29[b]	1.59[b]
≥ 65 years	2.57[b]	1.96[b]	2.68[b]	1.77[b]	2.11[b]
< 65 years	0.30	0.88	1.03	0.04	0.27
Neoplasms	2.34[b]	2.01[b]	1.40	0.75	0.97
Lung cancer	3.05[b]	2.19	1.82	0.39	1.11
Cardiovascular Diseases	0.19	0.72	1.31	1.31[b]	1.30[b]
Coronary artery disease	0.94	1.89[b]	1.68	1.50[b]	1.62[b]
Respiratory Diseases	5.98[b]	4.03[b]	7.73[b]	3.86[b]	5.24[b]
≥ 65 years	6.90[b]	4.33[b]	9.03[b]	4.64[b]	6.25[b]
Nonmalignant Digestive Diseases	−1.28	1.81	1.90	0.67	1.29
Other Nonaccidental Causes	5.14[b]	2.63[b]	3.93[b]	2.04[b]	2.49[b]
AIDS	7.43	2.92	3.40	0.51	0.99
Diabetes	7.50[b]	5.52[b]	7.59[b]	4.48[b]	4.98[b]
Renal diseases	0.25	−1.30	−1.66	−0.10	−0.55
Neurologic conditions	1.98	0.07	0.66	0.12	0.35
Accidents	3.38	−1.37	2.04	1.73	1.69

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=x) + \text{LOESS}(\text{year}) + \text{multiple weather variables} + \beta(\text{pollutant})$, where i is an indicator for day and x is the selected span (percent) (Appendix D). Sulfate data from the Sutton monitoring station were available only for 1986 to 1993. See Appendix D for the included weather variables.

[b] Corrected t value > 1.96.

nonaccidental causes for predicted $PM_{2.5}$ and predicted sulfate from $PM_{2.5}$, also evaluated at the 3-day mean.

Summary of the Results by Cause of Death

The results of these analyses for both age groups combined, evaluated at the 3-day mean, are summarized in Table 15. In addition, Appendices H through O (available on request from the Health Effects Institute and from the HEI web site) show the results across selected lags, indices of particle exposures (COH, extinction, predicted $PM_{2.5}$, Sutton sulfate, and predicted sulfate from $PM_{2.5}$) and separate results for the two age groups. The figures in these appendices show considerable variability in the estimates, with most of the 95% CIs overlapping. This phenomenon reflects the statistical noise inherent in these time-series analyses.

Across all the indices of particles, we observed no association between the different particle measurements and accidental deaths, and deaths from AIDS, renal diseases, and neurological conditions.

Deaths from all nonaccidental causes of death across the three lags were consistently associated with the continuously monitored indices of particle air pollution (Figure 6). When the effects of PM were assessed over the three days preceding and including each index day (3-day mean) we generally found stronger effects. In addition, the associations were larger for persons ≥ 65 years (Figure 7).

Results for deaths from neoplasms were not as consistent as with nonaccidental causes of death. Associations at the 3-day mean were found for COH and the extinction coefficient, but not for sulfate. A greater number of daily deaths from cancer among persons ≥ 65 years of age were found than among those < 65. Most of these associations were statistically significant. We did not find a positive association with lung cancer.

Deaths from cardiovascular and coronary artery diseases appeared to be associated more with the indices representing sulfate, especially at 1-day lag and the 3-day mean. Daily mortality was higher among the elderly than among persons < 65 years, but the results were not consistent across the various indices of particle air pollution.

We observed consistent associations at 1-day lag and the 3-day mean for deaths from respiratory illnesses, and the number of daily deaths among the elderly was generally

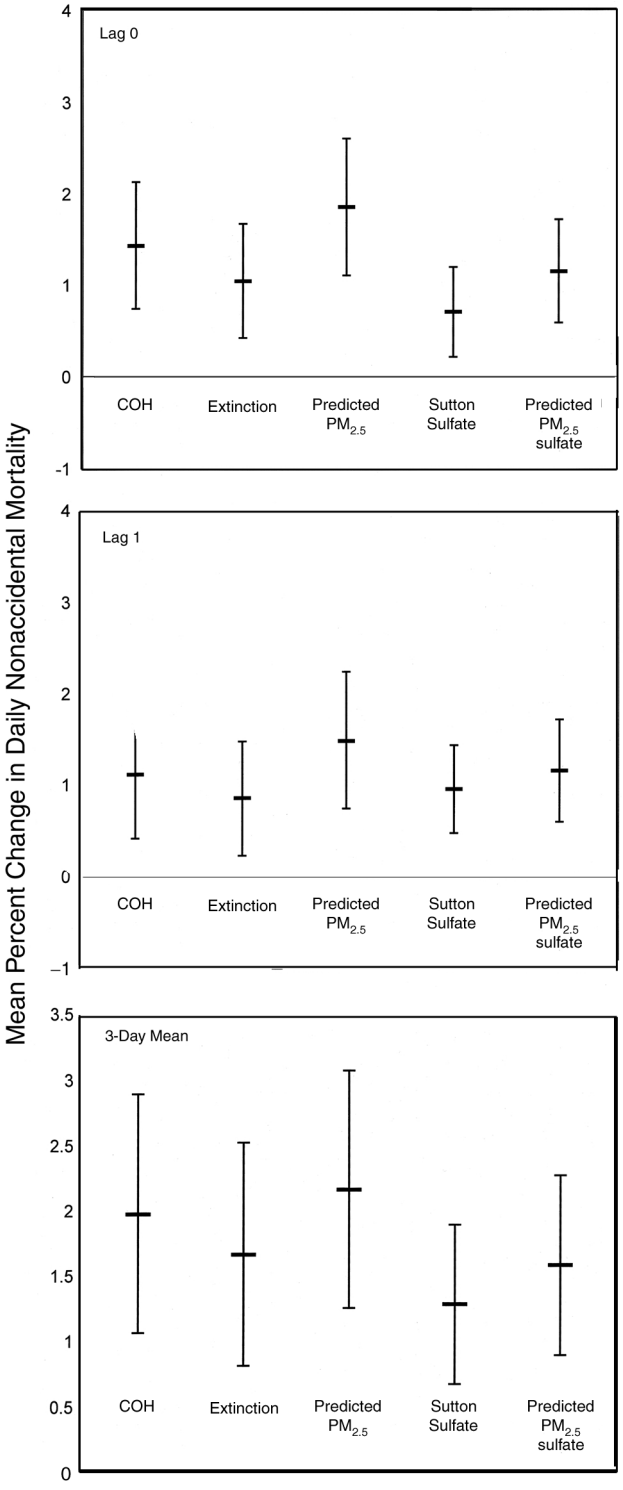

Figure 6. Mean percent change in daily nonaccidental mortality evaluated at lag 0, lag 1, and the 3-day mean for increase in ambient PM across each interquartile range. The bars represent the 95% confidence intervals on the mean percent change in daily mortality.

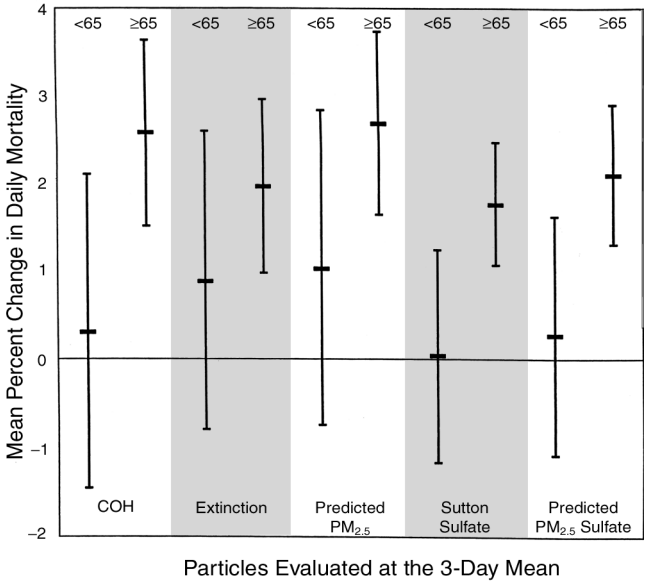

Figure 7. Mean percent change in daily nonaccidental mortality evaluated at the 3-day mean for increases in indices of ambient air particles across each interquartile range by age group (< 65 years and ≥ 65 years). The vertical bars represent the 95% confidence intervals on the mean percent change in daily mortality.

quite high. Deaths from diabetes were consistently associated with the indices of particle air pollution.

Sensitivity Analyses

We conducted a series of sensitivity analyses to determine whether the results reported above would be modified if we used different temporal filters, if we considered different weather variables, or if we included gaseous pollutants as covariates.

We found few important differences among the results for temporal filters having spans of 31/3,653 (0.8% of the data), 91/3,653 (2.5%), or 151/3,653 days (4.1%). The only aberrant result was for the association between neoplasms and $PM_{2.5}$, in which we found a much larger estimate for the 31-day span compared with the 151-day span (MPC = 4.00% and 1.12%, respectively).

Using the temporal filter selected for the primary analyses, we carried out analyses using the single weather variable that had the lowest AIC, and we conducted analyses without any adjustment for weather variables. Overall, the estimates did not change dramatically across the different models.

Table 12 shows the results for specified causes of death after adding gaseous pollutants separately and in combination to the statistical models for COH, predicted $PM_{2.5}$, and total sulfate from the Sutton station evaluated at the 3-day mean. Estimates of effect for nonaccidental causes of

death varied somewhat according to which pollutant was added to the model, with some pollutants increasing and others decreasing the estimates. Despite fluctuations in the estimates, the conclusions reached above for nonaccidental causes of death were not changed by the inclusion of any of the gaseous pollutants that we considered. For COH models, the inclusion of SO_2 decreased the estimates but the addition of O_3 generally increased the effects. For the analysis of Sutton sulfate and predicted $PM_{2.5}$, SO_2 had little effect on the results while the estimates of effect were generally reduced by O_3; this is likely due to the high positive correlation between these two pollutants (both had maxima in the summer period). Inclusion of the gaseous pollutants led to considerable variability in the results for diabetes. As the mean number of daily deaths was only 1.0 (Table 10), this variability may indicate that adjustments may not be appropriate for time series that are based on few numbers of deaths.

PART 2: IDENTIFICATION OF SUSCEPTIBLE GROUPS OF THE POPULATION

In this part of the report, we describe the analyses to identify persons with specific conditions before death who had higher than expected daily mortality when concentrations of ambient particles were increased. Following current hypotheses regarding mechanisms of action (Bates 1992; Seaton et al 1995; Goldberg 1996; Frank and Tankersley 1997), we focused on respiratory and cardiovascular illnesses. It has also been postulated that persons in poor and failing health may be at higher risk than those who are not frail (Goldberg 1996; Frank and Tankersley 1997). We analyzed cancer because of its systemic effects on the body and because we found increases in daily mortality for cancer.

We linked each deceased subject in the study population to QHIP records so as to obtain information regarding health conditions for the period five years before death. To define the disease group groups, we used medical services and procedures rendered, diagnosis provided by physicians on the billing record, and prescriptions filled for pharmaceuticals. We developed working definitions and wrote algorithms to identify persons with cancer, specific cardiovascular diseases, and respiratory conditions.

The health services data included fee-for-services provided by physicians that were reimbursable by the QHIP. These billings covered services rendered both in and out of hospital. (Laboratory tests, and the results from these tests, were not part of the database because they were not provided by physicians on a fee-for-service basis.) A physician submitting a bill for service had the option to record one diagnosis (ICD-9). Because the recording of a diagnosis was not mandatory, unlike the actual billing data, these data were not checked by the QHIP for consistency or accuracy. In addition, diagnoses were provided in only about half of the records. Because it is likely that most physicians used a restricted set of ICD-9 codes reflecting the mix of subjects that consulted them, their use of any one diagnostic code would not capture specific conditions (eg, asthma), but sets of related ICD-9 codes were considered adequate for indicating associated diseases (eg, airways disease). To increase the specificity of the indicators of disease group that we were considering, we thus made use of all types of information available on the databases: diagnoses, specific health services rendered, and prescriptions paid for by the QHIP.

The pharmaceutical database consisted of filled prescriptions that were reimbursed by the QHIP for persons ≥ 65 years of age and for individuals on social assistance. Because social assistance status can change with time, we decided to use only prescriptions among the elderly.

For eligible persons not in hospital, prescriptions for pharmaceuticals are covered by the QHIP. However, when hospitalized, prescriptions are paid for directly by the hospital for the duration of the patient's stay, and do not appear in the QHIP database. The major complications in using this database were that (1) the drug formulary changed with time, and (2) each type of pharmaceutical was identified by a set of Drug Identification Numbers (DINs). It was thus necessary to identify all associated DINs for each drug.

After we developed the indices, we carried out a series of informal validations. First, we compared our indicators of disease group with diagnostic codes listed for subjects who were hospitalized during the study period. Second, we selected a control group of nondeceased persons from the QHIP files in order to compare the odds of death for the various indicators of disease group. The expectation here was that fatal diseases, such as cancer, would show strong associations with mortality whereas less serious conditions, such as upper respiratory infections, would not.

Once the groups were created, we conducted time-series analyses linking levels of ambient particles with daily nonaccidental mortality within each group separately and also among subjects who appeared simultaneously in more than one group.

MATERIALS AND METHODS

Study Population

The study population consisted of all persons who died from nonaccidental causes (133,904 persons). In addition, we randomly selected a control group of 50,000 nonde-

ceased people from QHIP's nominal roll of persons who were living in Montreal, frequency-matched to the group of decedents by year of birth and sex. Because place of residence was available from the QHIP only from 1987 to 1993, we sampled approximately equal numbers of subjects from the QHIP's nominal roll for each of these years. (For deceased subjects, we used residences recorded on the death certificates.)

Development of Indicators of Disease Group

Data Sources For each subject in either group, we extracted data on services rendered by physicians and filled prescriptions for drugs from the QHIP's administrative files (Table 16). For the deceased population, we obtained data for the five-year period before death and, for the control group, for the five-year period before the year of their selection.

Table 16. Information Available from Billing and Pharmaceutical Databases of QHIP

Billing Database
Date of billing
Code for billing (services and procedures)
Diagnostic code (ICD-9)
Specialty of treating physician

Pharmaceutical Database[a]
Date of prescription
Medication (Drug Identification Number [DIN])
American Hospital Formulary (AHF) Service classification
Form of drug dispensed (eg, pills)
Dose
Quantity dispensed
Duration of prescription

[a] Data used only for persons ≥ 65 years and obtained for the 5 years before death.

Temporal Components Our goal was to uncover underlying health conditions close to the time of death that may have caused individuals to be susceptible to the effects of air pollution. The focus was primarily on chronic diseases, although we also included certain acute diseases, such as pneumonia and influenza, that may have required direct medical intervention. Two key factors in choosing appropriate time intervals were the typical time course of the diseases under consideration and the manner in which data were recorded on the billing and prescription databases.

Most chronic diseases are not curable and persist for months or years after initial detection, although treatment can modify their natural history and relieve symptoms. There will, of course, be considerable within- and between-subject variability in disease groups over time. We could not easily discern temporal variations in health status, although we could identify certain critical health events, such as strokes and acute myocardial infarctions.

We needed to account for the frequency by which diagnostic codes were entered onto the billing database as well as for the distribution of the duration of prescriptions for pharmaceuticals. In Quebec, the average duration of a prescription is about one month, so an interval of less than one month to define disease group would probably have led to a loss of important information. In addition, because physicians were not required to enter a diagnostic code, diagnoses were recorded on about half of the billing records. If an inordinate amount of time elapsed between rendered services, key diagnostic data could be lost. (On the other hand, persons hospitalized before death would have been more likely to receive multiple services than subjects who were not, so diagnoses would have been recorded more frequently.) In Quebec, the median duration of hospitalization for cardiovascular diseases was about 10 days (except for strokes, 22 days); for respiratory conditions it ranged between one and 11 days; and for cancer it was 12 days.

Given the idiosyncratic nature in which diagnoses were recorded and drugs were prescribed, as well as complex patterns in the utilization of health care services, we felt that a two-month interval was the minimum for which we could develop reasonably reliable indicators of disease. We also assumed that we could identify most chronic diseases by using an interval of six months to one year. For deceased subjects we defined three nested intervals of time prior to death in order to investigate the disease group indicators: two months, six months and one year.

For the control population, no critical point in time was available by which time intervals could be defined. Thus, we used either the date of the last medical interaction in the year in which the control subject was selected, or the last day of the year of selection if no medical interactions were recorded in that year. (The term *reference date* is used to represent this date for controls; for deceased subjects the reference date is the date of death.) We therefore assumed that reference dates for controls were equivalent to a random sample of dates and that these would provide unbiased comparisons of disease group between controls and deceased subjects.

Definition of Indicators of Disease Group Three sets of indicators were developed: respiratory conditions (developed by Drs Robert Levy and Pierre Ernst, McGill University; Table 17), cardiovascular conditions (developed by Dr

Table 17. Definitions for Respiratory Disease Groups

Age and Disease	Diagnoses (ICD-9 Codes)[a] in Specified Time Interval	Prescriptions[b] in Specified Time Interval	Services/Tests/ Procedures[a] in Specified Time Interval
Airways Disease			
< 65 and ≥ 65 years	Airways disease by a respirologist OR	None	None
	General practitioner OR	None	≥ 2 Sequential pulmonary function tests
≥ 65 years	Not diagnosed	Any prescription for bronchodilators (beta-agonists, etc), inhaled corticosteroids, systemic corticosteroids, anticholinergics, sodium chromoglycate (chromolyn), theophylline	None
Chronic Upper Respiratory (CUR)			
< 65 and ≥ 65 years	CUR	None	None
Acute Upper Respiratory (AUR)			
< 65 and ≥ 65 years	AUR	None	None
Acute Lower Respiratory (ALR)			
< 65 and ≥ 65 years	ALR	None	None

[a] See Appendix F for diagnoses used in the disease group definition.

[b] Data used only for persons ≥ 65 years.

Kenneth Flegel, McGill University; Tables 18 and 19), and cancer (developed by the first author of this report; Table 20).

Respiratory Diseases We defined separate indicators for chronic upper respiratory diseases, acute upper respiratory diseases, acute lower respiratory diseases, and airways disease (Tables 17 and F.2). Upper respiratory diseases were included as a control group, as we believed it implausible that associations would be found for this group. We relied solely on ICD-9 diagnostic codes reported on the billing record to define the first three entities while we made use of diagnoses, sequential pulmonary function tests, and prescriptions (only in persons ≥ 65 years) to define airways disease. (The distribution of diagnoses for each disease group is given in Appendix F.)

In defining airways disease, we assumed that the data from the QHIP were not sufficiently specific to discriminate among asthma, chronic bronchitis, and emphysema. In addition, because clinicians did not follow well-defined standards in prescribing drugs, we decided not to discriminate by severity using dose or quantity of drugs filled. For persons ≥ 65 years, we classified a subject as having airways disease if a specific diagnosis was listed, if two or more sequential pulmonary function tests were conducted, and if prescriptions were filled for any of the listed drugs. Subjects classified as having airways disease based solely on a filled prescription for systemic corticosteroids may have been misclassified, so we also created a group that excluded subjects who had only this type of prescription.

Cardiovascular Diseases We defined the following indices of cardiovascular disease group (Table 18, Table F.1): hypertension, congestive heart failure, acute coronary artery disease, chronic coronary artery diseases, cerebrovascular diseases, and chronic rheumatic heart diseases. We developed a specific index to identify coronary bypass procedures and this was combined with chronic and acute coronary artery disease to form a composite index referred to as *any coronary artery disease* (Table 19). Another composite index included all of these cardiovascular indices (referred to as *any cardiovascular disease*).

Cancer The definition of cancer (Table 20) included any diagnosis for a neoplasm (ICD-9 codes 140–239) and surgical and chemotherapeutic procedures specified to be for

Table 18. Definitions for Cardiovascular Disease Groups[a]

Age and Disease	Diagnoses (ICD-9 Codes) in Specified Time Interval[b]	Prescriptions[c] in Specified Time Interval	Services/Tests/Procedures in Specified Time Interval
Hypertension			
< 65 years	High BP ≥ 3 billings	None	None
≥ 65 years	High BP ≥ 3 billings	None	None
	OR		
	High BP ≥ 2 billings	Any prescription for diuretics, beta-blockers, calcium channel inhibitors, ACE inhibitors, vasodilators	None
Congestive Heart Failure			
< 65 years	CHF ≥ 2 billings	None	None
≥ 65 years	CHF ≥ 2 billings	None	None
	OR		
	CHF ≥ 1 billing	Any prescription for diuretics	None
Acute Coronary Artery Disease			
All ages	Acute MI	None	None
Chronic Coronary Artery Disease			
< 65	CCAD	None	Coronary catheterization or stress test
	OR		
	CCAD ≥ 3 billings	None	None
	OR		
	CCAD diagnosed by a cardiologist	None	None
≥ 65	CCAD	None	≥ 1 Coronary catheterization or stress test
	OR		
	CCAD ≥ 3 billings	None	None
	OR		
	CCAD diagnosed by a cardiologist	None	None
	OR		
	CCAD	≥ 2 Prescriptions for nitroglycerine	None
Coronary Artery Bypass (chronic or acute)		None	≥ 1 PTCA (angioplasty) OR coronary bypass
Cerebrovascular Diseases			
All ages	Stroke	None	None
Chronic Rheumatic Heart Disease			
All ages	CRHD	None	None

[a] ACE = acute coronary event; CCAD = chronic coronary artery disease; CHF = congestive heart failure; CRHD = chronic rheumatic heart disease; ECG = electrocardiogram; MI = myocardial infarction; and PTCA = percutaneous transluminal coronary angioplasty.

[b] See Appendix F for diagnoses used in the disease group definition.

[c] Data used only for persons ≥ 65 years.

Table 19. Composite Cardiovascular Indices

Composite Index	Specific Cardiovascular Indices Included in the Composite
Any coronary artery disease	Acute coronary disease Chronic coronary disease Coronary artery bypass
Any cardiovascular disease	Acute coronary disease Chronic coronary disease Hypertension Coronary artery bypass Congestive heart failure Cerebrovascular disease Chronic rheumatic heart disease

cancer, and prescription of the entire class of cancer chemotherapeutic agents (American Hospital Formulary Service [AHFS] class 10:00).

Combining Groups Because most subjects within each of the above groups had a variety of comorbid conditions, we created seven mutually exclusive groups composed of subjects having combinations of the presence or absence of any cardiovascular conditions, acute and chronic lower respiratory diseases (excluding lung cancer), and cancer. In addition, we created one other group that consisted of individuals who did not have cardiovascular or lower respiratory diseases (including respiratory cancer).

Table 20. Definitions for the Cancer Group

Age and Disease	Diagnoses (ICD-9 Codes) in Specified Time Interval	Prescriptions[a] in Specified Time Interval	Services/ Tests/ Procedures in Specified Time Interval
Cancer			
All ages	140–239 OR	None	None
	None	Antineoplastic agents	None
	OR		
	None	None	Cancer procedures, excluding radiotherapy

[a] Data used only for persons ≥ 65 years.

Group-Specific Statistical Analyses of the Effects of Particles on Daily Nonaccidental Mortality

After excluding all subjects who died from accidents, we created groups of subjects classified according to whether they had cancer, respiratory conditions, or cardiovascular diseases. These groups were created using data in three nested time intervals (two months, six months, and one year before death). Subjects could be placed into more than one group and those who were not attributed into any of these three groups were thus excluded from these analyses (but were included in the analyses of the combined groups; see below). Because of inconsistencies in reporting as well as changes over time in disease group, the same set of subjects would not necessarily be included in each group across the three nested time intervals.

We conducted separate time-series analyses for each group with the same statistical model that was used in the analyses of nonaccidental deaths (see Part 1):

$$\begin{aligned} E[\log(Y_i)] = {} & \alpha + \text{LOESS}(i, \text{span} = 91/3{,}653) \\ & + \text{LOESS}(\text{year}) \\ & + \text{LOESS}(\text{mean daily temperature}_{\text{lag}=0}, \text{change in barometric pressure from the previous day}_{\text{lag}=0}) \\ & + \beta\ (\text{particle index})_i\ , \end{aligned}$$

where i indicates the day in the time series and Y_i is the number of deaths on day i. The third LOESS term represents a smooth interaction surface between mean daily temperature and change in barometric pressure from the previous day. As before, we used quasi-likelihood to account for non-Poisson variation. We carried out analyses both by age group (< 65 years and ≥ 65 years) and by adjusting for SO_2 and O_3.

RESULTS

Study Population

We described the deceased population in Part 1 of this report. For the control group, we were aware that vital status on the QHIP's list was not recorded with perfect accuracy, and so we assessed whether any of these subjects had died in hospital. Linking these subjects to the hospital discharge database for the time period for which we had data (1990 to 1993), we discovered that 438 (0.9%) of them had died while in hospital, and these subjects were excluded from the study. Appendix F shows that the control group was closely frequency-matched to the deceased group.

Indicators of Disease Group

The deceased and comparison populations were evaluated in terms of the number of interactions with the Quebec health care system over the five-year interval before the reference date. The QHIP was able to provide data only from January 1980, so five years of data could not be obtained for all subjects who died in 1984. Two percent of deceased subjects and 8.8% of comparison subjects had no interactions with the health care system. On average, deceased subjects had twice as many billings as comparison subjects (146 and 70, respectively). Although about 50% of billing records had an associated diagnostic code, 87% of comparison subjects and 97% of deceased subjects had at least one diagnostic code attributed during the entire five-year time interval. In the elderly (≥ 65 years) a higher proportion of comparison subjects filled at least one prescription (87% versus 82%), but the mean number of filled prescriptions was higher in the deceased population (133 versus 114).

We used diagnostic codes as the main criterion for classifying subjects but rendered services and filled prescriptions made important contributions in defining chronic coronary artery disease (particularly in the elderly), congestive heart failure, hypertension, airways disease, and cancer. Three of the groups were defined only in terms of diagnostic codes (congestive heart failure < 65 years; acute coronary artery disease; hypertension < 65 years). A category labeled *no billings* refers to those individuals who had no interactions with the QHIP system. As expected from the overall age distribution, each group consisted mainly of subjects ≥ 65 years.

Selection of Time Intervals

We asked which time interval before death should be used in the substantive air pollution analyses. The proportions of subjects with at least one diagnostic code attributed in their billing record decreased considerably as the time window was decreased from five years to two months, suggesting that the choice of a short interval before death would exclude considerable information for identifying subjects with chronic diseases. The potential loss of information for using too small a time interval is illustrated with congestive heart failure among individuals ≥ 65 years of age. As many as 5,331 persons (38.4% of the 13,880 attributed within one year) would be excluded if the more stringent definition of the time interval of two months before death was used.

Our detailed analyses of these data (odds of death with respect to control group, agreement analyses with respect to hospital discharge data) suggested that information from the 12-month period before death should be used to define indices of chronic diseases (Tables F.6 through F.9, F.11, and F.12). However, the two-month time interval seemed to be a reasonable choice for identifying acute events that should affect mortality in the short-term (ie, acute upper or lower respiratory disease, acute coronary artery disease, and cerebrovascular disease).

Group-Specific Analyses of Mortality and Particle Air Pollution

Individual Groups We carried out separate analyses for all of the pollutants considered in Part 1. For particles that were monitored continuously (COH, extinction coefficient, predicted $PM_{2.5}$, sulfate from the Sutton station, sulfate from predicted $PM_{2.5}$), we conducted analyses for lag 0, lag 1, and the 3-day mean and, where numbers permitted, age-specific evaluations (< 65 and ≥ 65 years). As well, results are reported after we adjusted for the individual effects of SO_2 and O_3. Because of the reduced number of observations for those indices of ambient particles that were not measured continuously (TSP, $PM_{2.5}$, PM_{10}, sulfate from TSP, $PM_{2.5}$, and PM_{10}), we did not conduct analyses by age group and did not adjust for gaseous pollutants.

Table 21 shows the distribution of daily mortality by group, and it is apparent that numbers of deaths were low for *no billings* (ie, individuals who had no interactions with the QHIP system one year before death), chronic and acute upper respiratory diseases, and hypertension.

The results of all analyses (all indices of particles and lag periods) are included in Appendices H thorugh O (which are available on request from the Health Effects Institute and on the HEI web site). For this document, we report only results for COH, predicted $PM_{2.5}$, and sulfate from the Sutton station, all evaluated at the 3-day mean (Figures 8 through 17). Table 22 shows a summary of the findings for the 3-day mean across these selected indices of particles. We did not find any evidence of associations for the groups representing acute upper respiratory disease, chronic upper respiratory disease, airways disease, acute coronary artery disease, hypertension, or cerebrovascular disease. Although the data were fairly consistent in this regard (no associations were found at lag 0 or at lag 1),

Table 21. Distribution of Daily Nonaccidental Number of Deaths by Group, Montreal, 1984 to 1993

Disease Group	Total Number of Deaths	Number of Days with No Deaths	Mean	Variance	25th	50th	75th	100th
No Billings	5,204	894	1.4	1.5	1	1	2	8
Cancer	43,768	0	12.0	14.0	9	12	14	28
Respiratory Disease								
Acute upper respiratory disease	1,432	2,514	0.4	0.4	0	0	1	7
Chronic upper respiratory disease	2,541	1,869	0.7	0.8	0	0	1	6
Acute lower respiratory disease	15,775	85	4.3	6.0	2	4	6	17
Airways disease	29,030	7	7.9	11.0	6	8	10	23
Cardiovascular Disease								
Acute coronary artery disease	9,900	258	2.7	2.9	1	3	4	12
Chronic coronary artery disease	22,176	12	6.1	6.4	4	6	8	17
Congestive heart failure	16,794	61	4.6	5.5	3	4	6	16
Hypertension	7,977	468	2.2	2.4	1	2	3	10
Cerebrovascular diseases	10,861	207	3.0	3.3	2	3	4	13
Any coronary artery disease	29,209	3	8.0	8.8	6	8	10	20
Any cardiovascular disease	52,357	0	14.3	17.7	11	14	17	34

Table 22. Summary Estimates of the Mean Percent Change in Daily Nonaccidental Mortality for Selected Groups Defined by Billing and Prescription Data from QHIP for Their Respective Time Periods Before Death, for Three Measures of Particulate Matter Air Pollution, Across Interquartile Ranges and Evaluated at 3-Day Mean, Montreal, 1984 to 1993[a]

	Coefficient of Haze		Predicted $PM_{2.5}$		Sutton Sulfate	
Disease Group	Mean % Change[b]	95% CI	Mean % Change[b]	95% CI	Mean % Change[b]	95% CI
No Billings	0.84	–3.47, 5.33	4.70	0.32, 9.26	3.18	0.28, 6.17
Cancer	2.42	0.87, 4.00	1.84	0.33, 3.37	0.89	–0.12, 1.92
Respiratory Disease						
Acute upper respiratory disease	4.57	–4.06, 13.98	7.28	–1.12, 16.40	6.36	0.58, 12.47
Chronic upper respiratory disease	2.39	–3.78, 8.97	3.81	–2.19, 10.17	4.34	0.32, 8.51
Acute lower respiratory disease	5.09	2.47, 7.79	4.72	2.23, 7.28	2.25	0.56, 3.98
Airways disease	1.53	–0.39, 3.49	1.33	–0.45, 3.15	0.51	–0.72, 1.75
Cardiovascular Disease						
Acute coronary artery disease	2.35	–0.91, 5.70	2.27	–0.88, 5.52	0.99	–1.17, 3.19
Chronic coronary artery disease	2.62	0.53, 4.75	2.20	0.14, 4.31	0.63	–0.77, 2.06
Congestive heart failure	4.99	2.44, 7.60	4.02	1.61, 6.48	1.91	0.28, 3.56
Hypertension	3.35	–0.27, 7.10	1.88	–1.56, 5.44	0.53	–1.80, 2.92
Cerebrovascular disease	1.73	–1.35, 4.91	1.53	–1.40, 4.55	0.63	–1.37, 2.66
Any coronary artery disease	2.99	1.13, 4.88	1.85	0.03, 3.70	0.69	–0.55, 1.95
Any cardiovascular disease	3.65	2.23, 5.09	2.76	1.40, 4.15	1.16	0.23, 2.09

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=2.49\%) + \text{LOESS}(\text{year}) + \text{multiple weather variables} + \beta\ (\text{pollutant})$, where i is an indicator for day and x is the selected span (percent) (Appendix D). Sulfate data from the Sutton monitoring station were available only for 1986 to 1993. See Appendix D for the included weather variables.

[b] Mean percent change calculated for an increase of exposure equal to the interquartile value.

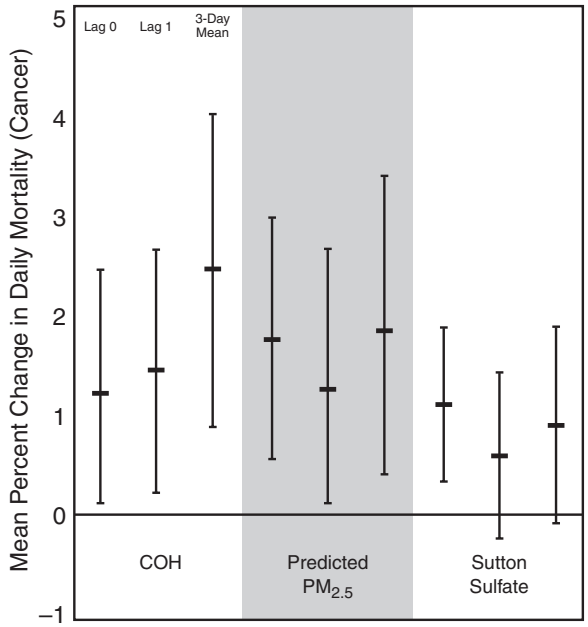

Figure 8. Mean percent change in daily mortality within cancer group for three measures of ambient PM evaluated at lag 0, lag 1, and 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

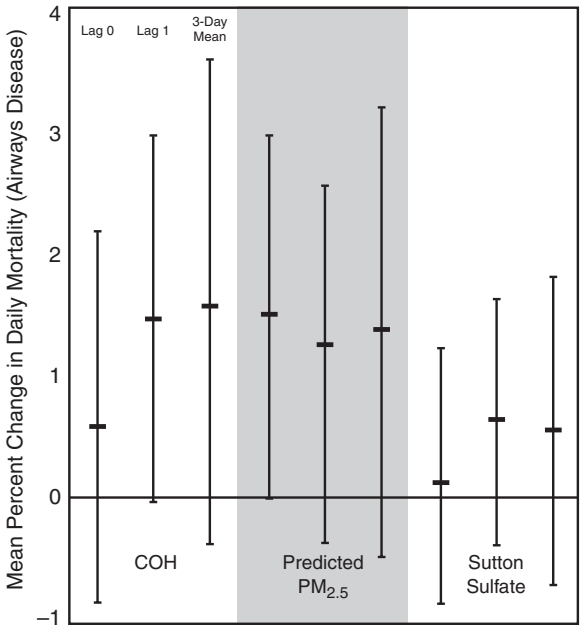

Figure 10. Mean percent change in daily mortality within airways disease group for three measures of PM evaluated at lag 0, lag 1, and 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

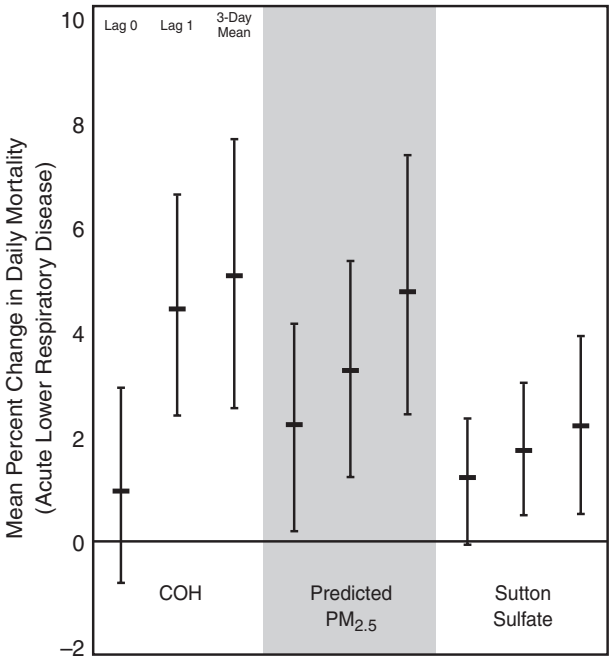

Figure 9. Mean percent change in daily mortality within acute lower respiratory disease group for three measures of PM evaluated at lag 0, lag 1, and 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

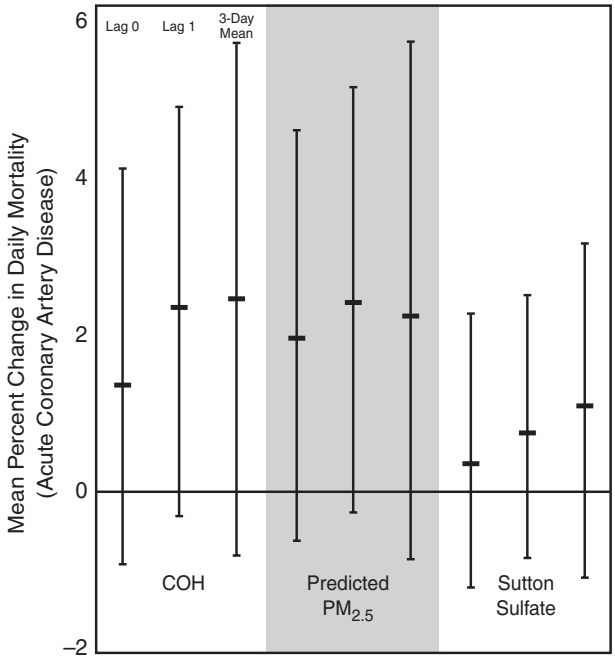

Figure 11. Mean percent change in daily mortality within acute coronary artery disease group for three measures of ambient PM evaluated at lag 0, lag 1, and 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

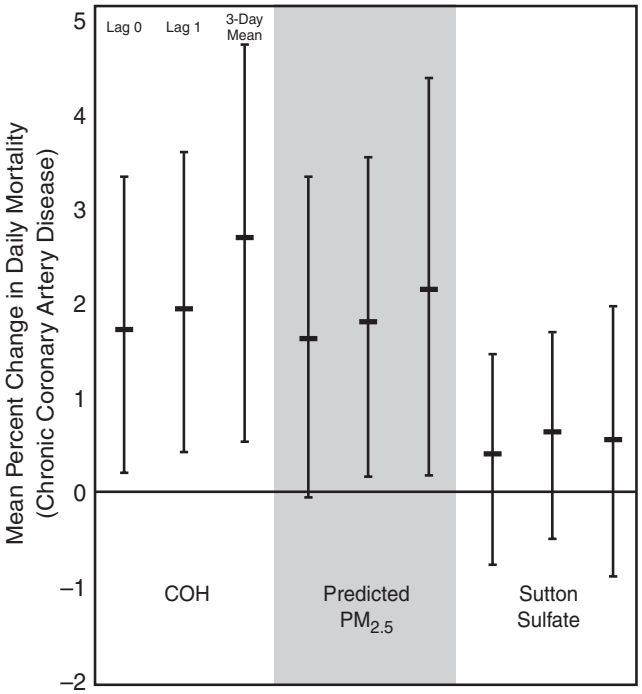

Figure 12. Mean percent change in daily mortality for chronic coronary artery disease group for three measures of ambient PM evaluated at lag 0, lag 1, and 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

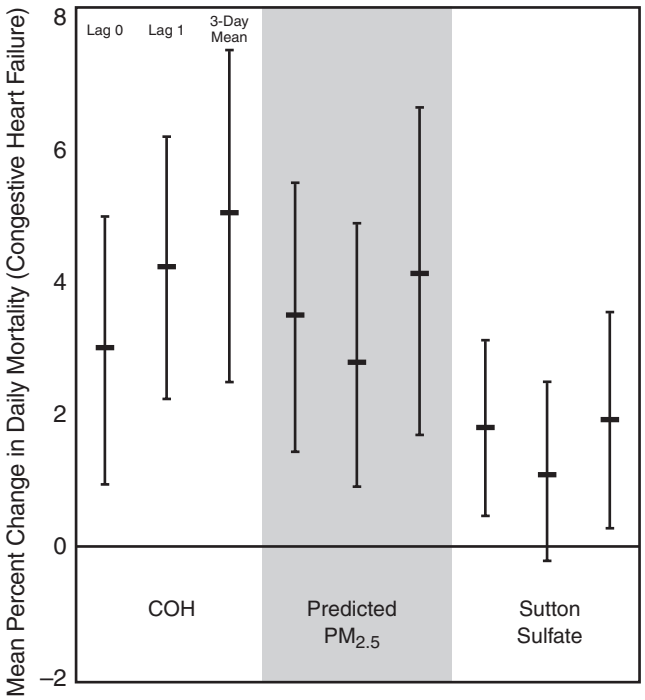

Figure 13. Mean percent change in daily mortality within congestive heart failure group for three measures of ambient PM evaluated at lag 0, lag 1, and 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

a few positive and statistically significant associations were found:

- Acute upper respiratory disease with sulfate from Sutton ($MPC_{3\text{-day mean}} = 6.36\%$).
- Chronic upper respiratory disease with sulfate from Sutton ($MPC_{3\text{-day mean}} = 4.34\%$).

For the very small no billings group, we found associations for predicted $PM_{2.5}$ and Sutton sulfate, and did not find any associations at lag 0 or lag 1 for any index of particles. We did not further analyze these groups because of the lack of evidence of an association. However, we were concerned that we might have missed effects in subjects ≥ 65 years who had had strokes and, because one of our a priori hypotheses was that persons with airways disease may be at higher risk, we conducted further in-depth analyses for these two groups.

We found positive associations for most indices of ambient particles monitored daily in the groups defined by cancer, acute lower respiratory disease, chronic coronary artery disease, congestive heart failure, any coronary artery disease, and any cardiovascular disease (Table 22, Figures 8 to 13). We found increased daily mortality among individuals ≥ 65 years who had cancer, acute lower respiratory disease, chronic coronary artery disease, and any cardiovascular diseases before death, which was not observed consistently among those < 65 years (Tables 23 and 24, Figures 14 to 17). We noted elevated risks among people ≥ 65 years with any coronary artery disease for the analyses of COH and predicted $PM_{2.5}$, (Table 24) but not for Sutton sulfate (Table 25). For COH, we found generally that adjusting for SO_2 decreased the MPCs and adjustments for O_3 increased the estimates, whereas, on the other hand, the reverse tendency was found when adjusting the effects of predicted $PM_{2.5}$ and Sutton sulfate.

Combined Groups The analyses described above included subjects with any of the indicators of disease group under consideration, regardless of their associated patterns of comorbidity. Many individuals near death will have more than one serious disease that lead inevitably to their demise. For example, some persons with cancer also had cardiovascular diseases (28%) and airways disease (28%); individuals with acute lower respiratory diseases also suffered from cardiovascular diseases (51%), airways disease (33%), and cancer (27%). Individuals with cardiovascular

Table 23. Mean Percent Change in Daily Nonaccidental Mortality for Coefficient of Haze Evaluated at the 3-Day Mean, Adjusted for Sulfur Dioxide and Ozone Separately, According to Groups Defined Using Billing and Prescription Data from QHIP, by Age Group, Montreal, 1984 to 1993[a]

	< 65 Years		≥ 65 Years		Total	
Disease and Pollutant Group	Mean % Change[b]	95% CI	Mean % Change[b]	95% CI	Mean % Change[b]	95% CI
Cancer						
Unadjusted	1.26	−1.32, 3.92	2.87	0.97, 4.81	2.42	0.87, 4.00
SO_2	0.72	−2.12, 3.64	2.64	0.54, 4.77	2.07	0.36, 3.81
O_3	1.12	−1.51, 3.82	3.44	1.50, 5.42	2.71	1.13, 4.32
Respiratory Disease						
Acute lower respiratory disease						
Unadjusted	4.02	−1.59, 9.95	5.32	2.35, 8.38	5.09	2.47, 7.79
SO_2	2.95	−3.16, 9.45	5.74	2.45, 9.14	5.19	2.29, 8.18
O_3	5.02	−0.74, 11.13	5.83	2.79, 8.96	5.71	3.02, 8.46
Airways disease						
Unadjusted	2.24	−3.23, 8.02	1.41	−0.63, 3.49	1.53	−0.39, 3.49
SO_2	1.07	−4.91, 7.43	1.17	−1.06, 3.45	1.18	−0.92, 3.32
O_3	2.18	−3.38, 8.05	0.93	−1.13, 3.04	1.09	−0.85, 3.07
Airways disease (excluding subjects taking drugs)						
Unadjusted	N/A		5.46	0.36, 10.83	N/A	
SO_2	N/A		5.70	−0.05, 11.78	N/A	
O_3	N/A		5.73	0.49, 11.24	N/A	
Airways disease (excluding only systemic corticosteroids)						
Unadjusted	N/A		0.93	−1.23, 3.15	N/A	
SO_2	N/A		0.70	−1.69, 3.14	N/A	
O_3	N/A		0.40	−1.80, 2.65	N/A	
Cardiovascular Disease						
Chronic coronary artery disease						
Unadjusted	−5.63	−10.30, −0.73	4.45	2.09, 6.85	2.62	0.53, 4.75
SO_2	−5.71	−10.85, −0.27	3.81	1.22, 6.47	2.09	−0.21, 4.45
O_3	−5.89	−10.64, −0.89	4.25	1.85, 6.69	2.44	0.31, 4.61
Congestive heart failure						
Unadjusted	N/A		5.65	2.90, 8.47	4.99	2.44, 7.60
SO_2	N/A		4.17	1.17, 7.26	3.77	0.98, 6.64
O_3	N/A		6.14	3.33, 9.01	5.45	2.85, 8.11
Cerebrovascular disease						
Unadjusted	N/A		0.70	−2.60, 4.12	1.73	−1.35, 4.91
SO_2	N/A		1.17	−2.47, 4.95	1.78	−1.61, 5.29
O_3	N/A		0.73	−2.62, 4.19	1.66	−1.47, 4.88
Any coronary artery disease						
Unadjusted	−2.97	−7.17, 1.41	4.33	2.25, 6.45	2.99	1.13, 4.88
SO_2	−2.88	−7.51, 1.99	3.86	1.57, 6.21	2.68	0.63, 4.77
O_3	−2.98	−7.25, 1.49	4.68	2.56, 6.85	3.29	1.39, 5.22
Any cardiovascular disease						
Unadjusted	0.49	−2.84, 3.93	4.31	2.75, 5.90	3.65	2.23, 5.09
SO_2	0.13	−3.53, 3.94	3.77	2.05, 5.52	3.13	1.57, 4.72
O_3	0.27	−3.11, 3.77	4.57	2.97, 6.19	3.83	2.38, 5.30

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=2.49\%) + \text{LOESS}(\text{year}) + \text{multiple weather variables} + \beta\ (\text{pollutant})$, where i is an indicator for day and x is the selected span (percent) (Appendix D). N/A = not analyzed. See Appendix D for the included weather variables.

[b] Mean percent change calculated for an increase of exposure equal to the interquartile value.

Table 24. Mean Percent Change in Daily Nonaccidental Mortality for Predicted $PM_{2.5}$ Evaluated at the 3-Day Mean, Adjusted for Sulfur Dioxide and Ozone Separately, According to Groups Defined Using Billing and Prescription Data from QHIP, by Age Group, Montreal, 1984 to 1993[a]

	< 65 Years		≥ 65 Years		Total	
Disease and Pollutant Group	Mean % Change[b]	95% CI	Mean % Change[b]	95% CI	Mean % Change[b]	95% CI
Cancer						
Unadjusted	0.98	−1.55, 3.57	2.21	0.39, 4.06	1.84	0.33, 3.37
SO_2	0.60	−2.09, 3.35	2.32	0.38, 4.30	1.78	0.17, 3.41
O_3	0.76	−1.78, 3.36	1.99	0.17, 3.84	1.60	0.09, 3.14
Respiratory Disease						
Acute lower respiratory disease						
Unadjusted	4.35	−0.96, 9.94	4.73	1.91, 7.63	4.72	2.23, 7.28
SO_2	3.42	−2.20, 9.35	5.02	2.00, 8.13	4.74	2.07, 7.47
O_3	4.16	−1.15, 9.76	4.73	1.91, 7.63	4.68	2.19, 7.24
Airways disease						
Unadjusted	2.47	−2.66, 7.87	1.07	−0.82, 3.00	1.33	−0.45, 3.15
SO_2	1.94	−3.49, 7.68	1.18	−0.85, 3.24	1.35	−0.56, 3.28
O_3	1.76	−3.35, 7.15	0.43	−1.45, 2.35	0.60	−1.17, 2.40
Airways disease (excluding subjects taking drugs)						
Unadjusted	N/A		4.12	−0.90, 9.38	N/A	
SO_2	N/A		4.31	−1.04, 9.95	N/A	
O_3	N/A		3.87	−1.13, 9.12	N/A	
Airways disease (excluding only systemic corticosteroids)						
Unadjusted	N/A		1.25	−0.79, 3.34	N/A	
SO_2	N/A		1.58	−0.61, 3.81	N/A	
O_3	N/A		0.64	−1.39, 2.71	N/A	
Cardiovascular Disease						
Chronic coronary artery disease						
Unadjusted	−2.84	−7.71, 2.28	3.16	0.88, 5.49	2.20	0.14, 4.31
SO_2	−2.84	−8.02, 2.63	2.75	0.33, 5.23	1.85	−0.34, 4.09
O_3	−1.47	−6.40, 3.72	2.42	0.15, 4.73	1.76	−0.29, 3.86
Congestive heart failure						
Unadjusted	N/A		4.24	1.65, 6.89	4.02	1.61, 6.48
SO_2	N/A		3.34	0.60, 6.15	3.48	0.92, 6.10
O_3	N/A		3.77	1.19, 6.41	3.50	1.10, 5.95
Cerebrovascular disease						
Unadjusted	N/A		0.80	−2.34, 4.05	1.53	−1.40, 4.55
SO_2	N/A		0.60	−2.74, 4.06	0.92	−2.19, 4.12
O_3	N/A		0.38	−2.76, 3.62	1.05	−1.87, 4.06
Any coronary artery disease						
Unadjusted	−0.41	−4.77, 4.15	2.34	0.33, 4.39	1.85	0.03, 3.70
SO_2	−0.21	−4.86, 4.66	2.04	−0.10, 4.22	1.70	−0.23, 3.68
O_3	0.41	−3.98, 5.01	1.91	−0.10, 3.95	1.65	−0.16, 3.50
Any cardiovascular disease						
Unadjusted	1.29	−2.07, 4.77	2.91	1.41, 4.42	2.76	1.40, 4.15
SO_2	0.75	−2.81, 4.43	2.87	1.28, 4.49	2.52	1.07, 3.99
O_3	1.32	−2.04, 4.80	2.72	1.22, 4.24	2.60	1.23, 3.99

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=2.49\%) + \text{LOESS}(\text{year}) + \text{LOESS}(\text{Mean temperature}_0, \text{Change in barometric pressure from the previous 24 hours}_0) + \text{LOESS}(\text{gaseous pollutant}_0) + \beta\ (\text{particle pollutant})$, where i is an indicator for day. N/A = not analyzed. See Appendix D for the included weather variables.

[b] Mean percent change calculated for an increase of exposure equal to the interquartile value.

Table 25. Mean Percent Change in Daily Nonaccidental Mortality for Sulfate Evaluated at the 3-Day Mean at Sutton, Adjusted for Sulfur Dioxide and Ozone Separately, According to Groups Defined Using Billing and Prescription Data from Quebec Health Insurance Plan, by Age Group, Montreal, 1986 to 1993[a]

	< 65 Years		≥ 65 Years		Total Years	
Disease and Pollutant Group	MPC[b]	95% CI	MPC[b]	95% CI	MPC[b]	95% CI
Cancer						
Unadjusted	0.01	–1.69, 1.75	1.39	0.17, 2.63	0.89	–0.12, 1.92
SO_2	–0.06	–1.79, 1.69	1.42	0.18, 2.67	0.94	–0.08, 1.98
O_3	–0.12	–1.89, 1.68	0.97	–0.29, 2.25	0.58	–0.47, 1.64
Respiratory Disease						
Acute lower respiratory disease						
Unadjusted	1.74	–1.88, 5.50	2.29	0.36, 4.25	2.25	0.56, 3.98
SO_2	1.57	–2.09, 5.37	2.32	0.37, 4.30	2.23	0.50, 3.98
O_3	1.93	–1.83, 5.82	2.15	0.16, 4.17	2.14	0.38, 3.93
Airways disease						
Unadjusted	0.23	–3.23, 3.81	0.50	–0.80, 1.82	0.51	–0.72, 1.75
SO_2	0.09	–3.41, 3.72	0.54	–0.78, 1.88	0.48	–0.76, 1.74
O_3	–0.13	–3.72, 3.60	–0.10	–1.44, 1.26	–0.10	–1.36, 1.18
Airways disease (excluding subjects taking drugs)						
Unadjusted	N/A		0.50	–2.94, 4.06	N/A	
SO_2	N/A		0.34	–3.14, 3.94	N/A	
O_3	N/A		–0.10	–3.63, 3.56	N/A	
Airways disease (excluding only systemic corticosteroids)						
Unadjusted	N/A		0.63	–0.78, 2.06	N/A	
SO_2	N/A		0.66	–0.77, 2.12	N/A	
O_3	N/A		0.08	–1.36, 1.55	N/A	
Cardiovascular Disease						
Chronic coronary artery disease						
Unadjusted	–0.26	–3.71, 3.32	0.84	–0.71, 2.41	0.63	–0.77, 2.06
SO_2	–0.20	–3.70, 3.43	0.71	–0.85, 2.30	0.58	–0.84, 2.03
O_3	0.30	–3.27, 4.00	0.24	–1.35, 1.86	0.25	–1.20, 1.72
Congestive heart failure						
Unadjusted	N/A		1.91	0.17, 3.69	1.91	0.28, 3.56
SO_2	N/A		1.69	–0.07, 3.49	1.72	0.08, 3.40
O_3	N/A		1.49	–0.31, 3.33	1.31	–0.37, 3.01
Cerebrovascular disease						
Unadjusted	N/A		0.56	–1.60, 2.76	0.63	–1.37, 2.66
SO_2	N/A		0.51	–1.67, 2.75	0.49	–1.53, 2.55
O_3	N/A		–0.01	–2.23, 2.27	0.11	–1.95, 2.21
Any coronary artery disease						
Unadjusted	0.98	–2.06, 4.11	0.57	–0.80, 1.96	0.69	–0.55, 1.95
SO_2	1.11	–1.98, 4.29	0.59	–0.79, 2.00	0.70	–0.55, 1.98
O_3	1.09	–2.06, 4.33	0.09	–1.32, 1.52	0.26	–1.02, 1.55
Any cardiovascular disease						
Unadjusted	0.30	–2.00, 2.65	1.33	0.32, 2.35	1.16	0.23, 2.09
SO_2	0.20	–2.12, 2.58	1.36	0.33, 2.40	1.17	0.23, 2.12
O_3	0.16	–2.22, 2.59	1.05	0.00, 2.11	0.90	–0.05, 1.87

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=2.49\%) + \text{LOESS}(\text{year}) + \text{LOESS}(\text{Mean temperature}_0, \text{Change in barometric pressure from the previous 24 hours}_0) + \text{LOESS}(\text{gaseous pollutant}_0) + \beta\ (\text{particle pollutant})$, where i is an indicator for day. Sulfate data from the Sutton monitoring station were available only for 1986 to 1993. N/A = not analyzed. See Appendix D for the included weather variables.

[b] Mean percent change calculated for an increase of exposure equal to the interquartile value.

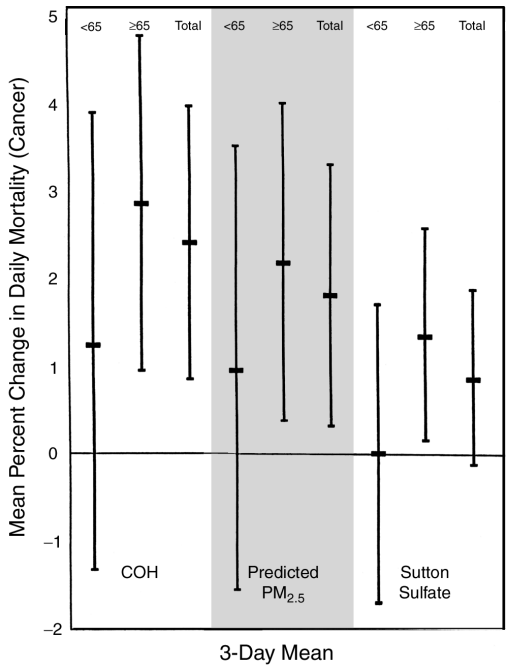

Figure 14. Mean percent change in daily mortality within cancer group for three measures of ambient PM by age group at the 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

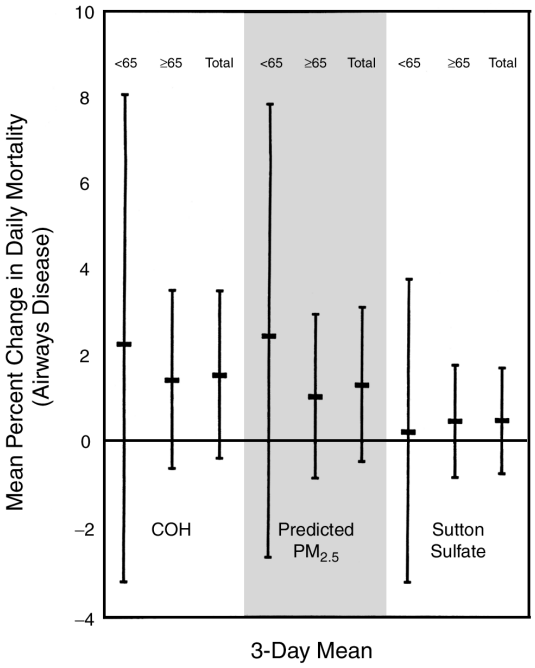

Figure 16. Mean percent change in daily mortality within airways disease group for three measures of ambient PM by age group at the 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

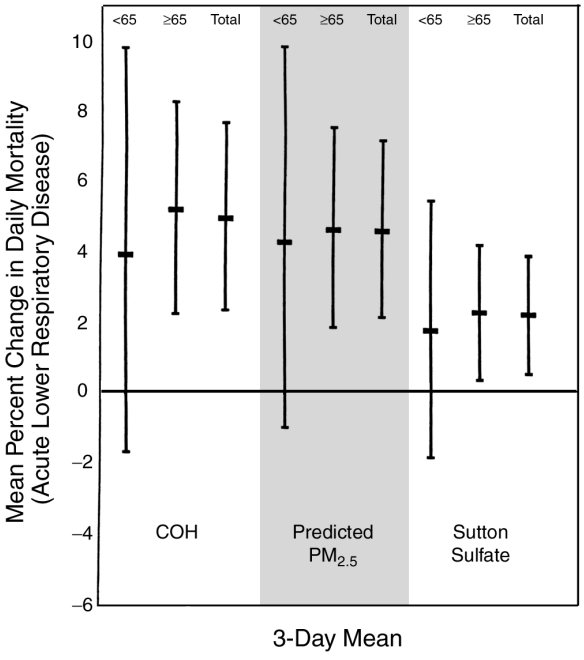

Figure 15. Mean percent change in daily mortality within acute lower respiratory disease group for three measures of PM by age group at the 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

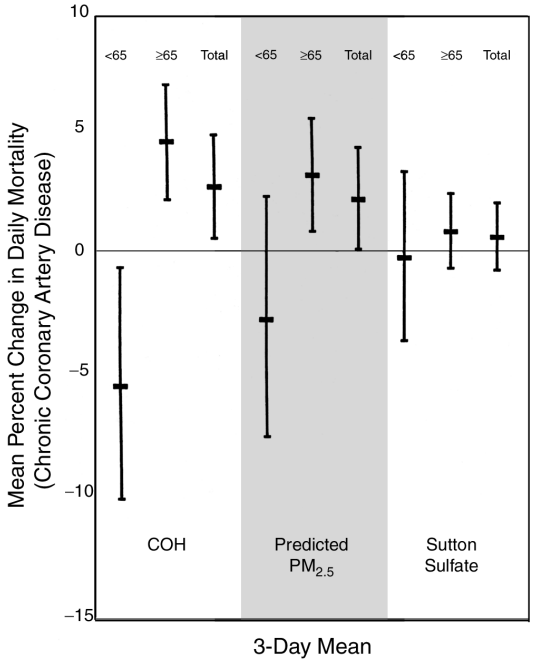

Figure 17. Mean percent change in daily mortality within chronic coronary artery disease group for three measures of ambient particulate matter by age group at the 3-day mean. The ordinate is in percent change in daily mortality for an increase equal to the interquartile range, and the vertical bars surrounding the point estimates are the 95% confidence limits. The horizontal line through the graph represents no association.

Table 26. Distribution of Daily Nonaccidental Mortality for Each Combined Group, Montreal, 1984 to 1993

Combined Disease Group	Total Number of Deaths	Number of Days with No Deaths	Mean	Variance	Percentile			
					25th	50th	75th	100th
No history of cardiovascular and respiratory diseases, including respiratory cancer	47,321	0	13.0	15.9	10	13	16	46
No cancer, no cardiovascular, no lower respiratory	39,133	0	10.7	13.7	8	10	13	42
Cancer only	22,468	8	6.2	6.4	4	6	8	15
Lower respiratory only	10,880	206	3.0	3.2	2	3	4	12
Lower respiratory and cancer	8,826	371	2.4	2.7	1	2	3	10
Cardiovascular only	26,793	0	7.3	7.7	5	7	9	21
Cardiovascular and cancer	7,732	456	2.1	2.2	1	2	3	9
Cardiovascular and lower respiratory	13,330	142	3.6	4.3	2	3	5	17
Cardiovascular and lower respiratory and cancer	4,742	1,123	1.3	1.6	0	1	2	10

Table 27. Summary Estimates of Mean Percent Change in Daily Nonaccidental Mortality for Combinations of Groups Defined Using Billing and Prescription Data from QHIP for Their Respective Time Periods Before Death, Across Interquartile Range of Lagged Exposure Evaluated at the 3-Day Mean to Three Measures of Particulate Matter, Montreal, 1984 to 1993[a]

Combined Disease Group	COH		Predicted $PM_{2.5}$		Sutton Sulfate	
	MPC[b]	95% CI	MPC[b]	95% CI	MPC[b]	95% CI
No cancer, no cardiovascular, no lower respiratory	0.31	−1.33, 1.97	2.27	0.59, 3.97	2.17	1.04, 3.32
Cancer only	1.60	−0.54, 3.78	1.03	−1.07, 3.17	0.84	−0.57, 2.28
Lower respiratory only	1.59	−1.35, 4.61	3.39	0.45, 6.42	1.52	−0.51, 3.58
Lower respiratory and cancer	3.51	0.07, 7.07	2.66	−0.58, 6.01	0.85	−1.34, 3.09
Cardiovascular only	4.16	2.22, 6.14	2.83	0.91, 4.78	1.22	−0.08, 2.54
Cardiovascular and cancer	2.18	−1.44, 5.93	1.76	−1.65, 5.28	0.84	−1.43, 3.16
Cardiovascular and lower respiratory	3.31	0.56, 6.13	2.79	0.17, 5.48	1.18	−0.62, 3.02
Cardiovascular and lower respiratory and cancer	2.84	−1.97, 7.88	3.07	−1.36, 7.71	1.28	−1.72, 4.38

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=2.49\%) + \text{LOESS}(\text{year}) + \text{LOESS}(\text{Mean temperature}_0, \text{Change in barometric pressure from the previous 24 hours}_0) + \beta\,(\text{pollutant})$, where y_i is the number of nonaccidental deaths on day i for subjects included in each group. Sulfate data from the Sutton monitoring station were available only for 1986 to 1993. See Appendix D for the included weather variables.

[b] Mean percent change calculated for an increase in exposure equal to the interquartile value.

diseases also had a wide variety of other conditions, such as cancer and airways disease (24%), diabetes (17%), renal diseases (11%), and neurological conditions (13%).

We describe below a series of analyses for groups that were defined from the eight possible combinations of subjects having cancer, lower respiratory diseases, or cardiovascular diseases (Table 26). We also created a ninth group consisting of subjects who, within the previous year, had no history of cardiovascular or respiratory diseases (including respiratory cancer; 47,321 subjects). (Complete results of combined group analyses are in Appendix N, which is available on request from the Health Effects Institute and on the HEI web site.)

Statistical power was limited for all analyses using Sutton sulfate as a metric for ambient particles, as two years of data were missing; and also for the combined groups of lower respiratory and cancer (8,826 deaths), cardiovascular and cancer (7,732 deaths), and cardiovascular diseases, lower respiratory disorders, and cancer (4,742 deaths). We found no evidence of associations for these groups.

The group whose subjects had no cancer, cardiovascular diseases, or lower respiratory diseases showed associations with predicted $PM_{2.5}$ and with Sutton sulfate, but not with COH (Table 27). For the former two pollutants, increased daily mortality was found generally in persons ≥ 65 years (Tables 28 through 30) and adjustments for the gaseous pollutants did not alter these results. These results suggest that there may be other subpopulations that we did not consider who may be susceptible to the effects of ambient particles, including subjects who had potentially fatal conditions (60%), including AIDS, atherosclerosis, dysrhythmias, diabetes, renal diseases, neurological conditions, dementia, and liver disease.

For the remainder of the groups, we found in the analysis of Sutton sulfate (Table 30) no evidence for associations, except possibly for persons only with lower respiratory conditions. As indicated above, this may have been due partly to reduced statistical power from the loss of two years of data. For predicted $PM_{2.5}$ and COH, we observed associations for persons only having cardiovascular diseases and those having cardiovascular diseases and lower respiratory illnesses. In addition, for COH, an association with lower respiratory diseases and cancer was found and, for predicted $PM_{2.5}$, an association with lower respiratory diseases only (Table 29) was observed.

DISCUSSION

CAUSE-SPECIFIC MORTALITY

A principal finding of this investigation was that the daily mean number of nonaccidental deaths was higher when daily levels of pollutants were increased. We considered three time periods before death for characterizing ambient particles (0-day lag, 1-day lag, and the 3-day mean). For some or all of these lags, statistically significant positive associations were found for COH, the extinction coefficient, TSP, predicted $PM_{2.5}$, and sulfate. Although daily mortality was also elevated for measured $PM_{2.5}$, the 95% CIs included the null value, and this may have been due to the relatively low power arising from a limited number of observations. The magnitude of associations on the day of death (lag 0) did not differ in the two age groups (< 65 years and ≥ 65 years), but larger effects in the elderly were found when pollutants were included in the models as the 3-day mean.

Deaths from neoplastic diseases also increased as most indices of particles increased, although the effect for sulfate was reduced somewhat when the 3-day mean was used. People ≥ 65 years were at increased risk when the 3-day mean was considered, but this was less apparent at lag 0. Associations for lung cancer were evident only for COH and for TSP evaluated at lag 0. No differences between the two age groups were found, except for a remarkable increase in deaths among the elderly as levels of sulfate increased.

Daily mortality from cardiovascular diseases increased across all indices of particles, but only for sulfate evaluated at the 3-day mean were the associations statistically significant. These associations were stronger in subjects ≥ 65 years. We noted associations between coronary artery diseases (acute and chronic) and particles, especially at the 3-day mean and among those ≥ 65 years.

Statistically significant associations for deaths from respiratory diseases and other nonaccidental causes, including diabetes, were consistently high (especially at the 3-day mean). For respiratory diseases we found stronger effects among the elderly than for all ages combined. Because this is the first report of an association with diabetes and because there are very few reported time-series analyses of cause-specific mortality, these results must be treated cautiously. Deaths from nonmalignant digestive diseases were also elevated when TSP, $PM_{2.5}$, and sulfate were assessed on the concurrent day, but no effects were found for exposures evaluated on the preceding days.

In these analyses we used a simple parametric linear term to represent the pattern of exposure to particles and daily

Table 28. Mean Percent Change in Daily Nonaccidental Mortality for Coefficient of Haze Evaluated at the 3-Day Mean, Adjusted for Sulfur Dioxide and Ozone Separately, according to Combinations of Groups Defined Using Billing and Prescription Data from QHIP, by Age Group, Montreal, 1984 to 1993[a]

	< 65 Years		≥ 65 Years		Total	
Combined Disease Group	MPC[b]	95% CI	MPC[b]	95% CI	MPC[b]	95% CI
No Cancer, No Cardiovascular, No Lower Respiratory						
Unadjusted	−1.25	−4.60, 2.22	0.74	−1.12, 2.63	0.31	−1.33, 1.97
SO_2	−1.87	−5.55, 1.94	−0.31	−2.34, 1.76	−0.52	−2.31, 1.30
O_3	−2.48	−5.85, 1.01	0.27	−1.62, 2.19	−0.28	−1.93, 1.41
Cancer Only						
Unadjusted	0.49	−2.80, 3.89	2.26	−0.51, 5.10	1.60	−0.54, 3.78
SO_2	0.78	−2.86, 4.55	2.04	−1.00, 5.17	1.57	−0.78, 3.98
O_3	0.46	−2.89, 3.92	2.98	0.16, 5.88	1.99	−0.19, 4.21
Lower Respiratory Only						
Unadjusted	N/A		2.17	−1.20, 5.65	1.59	−1.35, 4.61
SO_2	N/A		2.11	−1.62, 5.98	1.48	−1.78, 4.84
O_3	N/A		1.97	−1.47, 5.52	1.39	−1.60, 4.48
Lower Respiratory and Cancer						
Unadjusted	N/A		3.50	−0.81, 7.99	3.51	0.07, 7.07
SO_2	N/A		4.50	−0.29, 9.53	3.44	−0.36, 7.38
O_3	N/A		4.64	0.23, 9.24	4.10	0.59, 7.74
Cardiovascular Only						
Unadjusted	−0.40	−4.91, 4.33	4.98	2.86, 7.13	4.16	2.22, 6.14
SO_2	0.34	−4.69, 5.63	4.52	2.19, 6.90	3.86	1.72, 6.05
O_3	−1.07	−5.64, 3.73	5.83	3.66, 8.04	4.75	2.76, 6.77
Cardiovascular and Cancer						
Unadjusted	N/A		3.11	−0.96, 7.36	2.18	−1.44, 5.93
SO_2	N/A		1.77	−2.67, 6.41	1.15	−2.81, 5.27
O_3	N/A		3.34	−0.81, 7.66	2.35	−1.33, 6.17
Cardiovascular and Lower Respiratory						
Unadjusted	N/A		3.64	0.64, 6.73	3.31	0.56, 6.13
SO_2	N/A		3.56	0.24, 6.98	2.92	−0.11, 6.04
O_3	N/A		2.75	−0.28, 5.88	2.65	−0.14, 5.52
Cardiovascular and Lower Respiratory and Cancer						
Unadjusted	N/A		2.65	−2.68, 8.26	2.84	−1.97, 7.88
SO_2	N/A		2.85	−3.01, 9.06	2.22	−3.03, 7.76
O_3	N/A		2.69	−2.71, 8.39	2.80	−2.08, 7.92

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=2.49\%) + \text{LOESS}(\text{year}) + \text{LOESS}(\text{Mean temperature}_0, \text{Change in barometric pressure from the previous 24 hours}_0) + \text{LOESS}(\text{gaseous pollutant}_0) + \beta\ (\text{particle pollutant})$, where *i* is an indicator for day. N/A = not analyzed. See Appendix D for the included weather variables.

[b] Mean percent change calculated for an increase of exposure equal to the interquartile value.

Table 29. Mean Percent Change in Daily Nonaccidental Mortality for Predicted $PM_{2.5}$ Evaluated at the 3-Day Mean, Adjusted for Sulfur Dioxide and Ozone Separately, According to Combinations of Groups Defined Using Billing and Prescription Data from QHIP, by Age Group, Montreal, 1984 to 1993[a]

	< 65 Years		≥ 65 Years		Total	
Combined Disease Group	MPC[b]	95% CI	MPC[b]	95% CI	MPC[b]	95% CI
No Cancer, No Cardiovascular, No Lower Respiratory						
Unadjusted	0.74	−2.73, 4.33	2.64	0.76, 4.56	2.27	0.59, 3.97
SO_2	0.25	−3.42, 4.06	2.61	0.61, 4.66	2.17	0.39, 3.98
O_3	−0.20	−3.65, 3.38	2.59	0.70, 4.51	2.09	0.41, 3.79
Cancer Only						
Unadjusted	1.13	−2.17, 4.55	0.83	−1.84, 3.58	1.03	−1.07, 3.17
SO_2	1.16	−2.35, 4.80	0.94	−1.91, 3.87	1.05	−1.18, 3.33
O_3	1.17	−2.15, 4.59	0.51	−2.16, 3.25	0.80	−1.30, 2.94
Lower Respiratory Only						
Unadjusted	N/A		4.61	1.24, 8.09	3.39	0.45, 6.42
SO_2	N/A		5.07	1.45, 8.82	3.66	0.51, 6.91
O_3	N/A		4.61	1.24, 8.10	3.26	0.32, 6.28
Lower Respiratory and Cancer						
Unadjusted	N/A		3.67	−0.43, 7.93	2.66	−0.58, 6.01
SO_2	N/A		4.51	0.12, 9.10	2.83	−0.63, 6.41
O_3	N/A		3.87	−0.23, 8.14	2.53	−0.71, 5.87
Cardiovascular Only						
Unadjusted	1.36	−3.40, 6.37	2.93	0.86, 5.04	2.83	0.91, 4.78
SO_2	1.38	−3.70, 6.73	2.93	0.73, 5.18	2.78	0.73, 4.86
O_3	1.63	−3.14, 6.64	3.21	1.13, 5.33	3.03	1.10, 4.99
Cardiovascular and Cancer						
Unadjusted	N/A		3.43	−0.39, 7.39	1.76	−1.65, 5.28
SO_2	N/A		3.22	−0.83, 7.44	1.61	−2.01, 5.37
O_3	N/A		3.11	−0.71, 7.07	1.34	−2.07, 4.86
Cardiovascular and Lower Respiratory						
Unadjusted	N/A		3.06	0.21, 5.99	2.79	0.17, 5.48
SO_2	N/A		2.83	−0.20, 5.96	2.38	−0.41, 5.25
O_3	N/A		1.90	−0.92, 4.80	1.84	−0.76, 4.51
Cardiovascular and Lower Respiratory and Cancer						
Unadjusted	N/A		1.86	−3.06, 7.02	3.07	−1.36, 7.71
SO_2	N/A		1.72	−3.50, 7.23	2.62	−2.08, 7.54
O_3	N/A		1.80	−3.11, 6.96	2.99	−1.45, 7.64

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=2.49\%) + \text{LOESS}(\text{year}) + \text{LOESS}(\text{Mean temperature}_0, \text{Change in barometric pressure from the previous 24 hours}_0) + \text{LOESS}(\text{gaseous pollutant}_0) + \beta\ (\text{particle pollutant})$, where i is an indicator for day. N/A = not analyzed. See Appendix D for the included weather variables.

[b] Mean percent change calculated for an increase of exposure equal to the interquartile value.

Table 30. Mean Percent Change in Daily Nonaccidental Mortality for Total Sulfate Measured at Sutton Station Evaluated at the 3-Day Mean, Adjusted for Sulfur Dioxide and Ozone Separately (3-Day Mean), According to Combinations of Groups Defined Using Billing and Prescription Data from QHIP, by Age Group, Montreal, 1986 to 1993[a]

	< 65 Years		≥ 65 Years		Total	
Combined Disease Group	MPC[b]	95% CI	MPC[b]	95% CI	MPC[b]	95% CI
No Cancer, No Cardiovascular, No Lower Respiratory						
Unadjusted	0.06	−2.27, 2.45	2.76	1.48, 4.05	2.17	1.04, 3.32
SO_2	−0.10	−2.45, 2.31	2.77	1.49, 4.08	2.16	1.02, 3.32
O_3	−0.29	−2.72, 2.19	2.75	1.42, 4.09	2.14	0.96, 3.32
Cancer Only						
Unadjusted	−0.29	−2.53, 1.99	1.47	−0.34, 3.31	0.84	−0.57, 2.28
SO_2	−0.27	−2.53, 2.04	1.55	−0.28, 3.42	0.87	−0.56, 2.33
O_3	−0.30	−2.61, 2.07	0.93	−0.94, 2.83	0.47	−1.00, 1.96
Lower Respiratory Only						
Unadjusted	N/A		2.49	0.17, 4.87	1.52	−0.51, 3.58
SO_2	N/A		2.45	0.11, 4.85	1.54	−0.52, 3.63
O_3	N/A		2.34	−0.06, 4.80	1.47	−0.63, 3.62
Lower Respiratory and Cancer						
Unadjusted	N/A		1.09	−1.66, 3.92	0.85	−1.34, 3.09
SO_2	N/A		1.26	−1.53, 4.14	0.91	−1.31, 3.17
O_3	N/A		0.74	−2.10, 3.66	0.48	−1.78, 2.79
Cardiovascular Only						
Unadjusted	0.75	−2.56, 4.18	1.30	−0.10, 2.72	1.22	−0.08, 2.54
SO_2	0.79	−2.58, 4.27	1.32	−0.10, 2.76	1.28	−0.04, 2.61
O_3	0.54	−2.87, 4.07	1.18	−0.27, 2.65	1.10	−0.25, 2.47
Cardiovascular and Cancer						
Unadjusted	N/A		1.76	−0.77, 4.34	0.84	−1.43, 3.16
SO_2	N/A		1.68	−0.87, 4.30	0.81	−1.49, 3.16
O_3	N/A		1.52	−1.10, 4.20	0.57	−1.78, 2.98
Cardiovascular and Lower Respiratory						
Unadjusted	N/A		1.50	−0.46, 3.49	1.18	−0.62, 3.02
SO_2	N/A		1.49	−0.50, 3.51	1.09	−0.74, 2.95
O_3	N/A		0.87	−1.15, 2.92	0.60	−1.26, 2.49
Cardiovascular and Lower Respiratory and Cancer						
Unadjusted	N/A		0.43	−2.93, 3.91	1.28	−1.72, 4.38
SO_2	N/A		0.39	−3.02, 3.91	1.11	−1.94, 4.24
O_3	N/A		0.16	−3.31, 3.75	1.18	−1.94, 4.40

[a] The statistical model was $E[\log(Y_i)] = \alpha + \text{LOESS}(i, \text{span}=2.49\%) + \text{LOESS}(\text{year}) + \text{LOESS}(\text{Mean temperature}_0, \text{Change in barometric pressure from the previous 24 hours}_0) + \text{LOESS}(\text{gaseous pollutant}_0) + \beta\ (\text{particle pollutant})$, where i is an indicator for day. N/A = not analyzed. See Appendix D for the included weather variables. Sulfate data from the Sutton monitoring station were available only for 1986 to 1993.

[b] Mean percent change calculated for an increase of exposure equal to the interquarile range.

mortality. We also investigated nonlinearities in the exposure-response function, using an approximate partial *F* test associated with the LOESS function, and found that four associations differed markedly from linearity: J-shaped relationships were found between all nonaccidental causes of death and COH and predicted $PM_{2.5}$ evaluated at the 3-day mean, and between all other nonaccidental causes for predicted $PM_{2.5}$ and predicted sulfate from $PM_{2.5}$ also evaluated at the 3-day mean. We have no simple explanations for these patterns, so they also need to be interpreted cautiously.

All of our results were based on quasi-likelihood regression models of daily counts of deaths, accounting for annual, seasonal, and subseasonal fluctuations in mortality as well as for short-term changes in climatic conditions. In a series of sensitivity analyses, we found that the results changed little when different temporal filters were used and when three different weather models were considered. However, adjustments for gaseous pollutants (O_3, NO, NO_2, CO , and SO_2) affected the estimates to a greater extent, although the direction of the changes in estimates was not always consistent; for example, in the analysis of all nonaccidental deaths and COH, adjustments for O_3 increased the estimates by 15% and, for SO_2, the estimates were attenuated by 23%.

COMPARISON WITH PUBLISHED RESULTS

Montreal has relatively low levels of air pollution compared with most large urban centers in the world. It is important, both from scientific and regulatory perspectives, to determine whether the slope of the exposure-response function estimated from this study is comparable to those found in reports from more polluted areas than Montreal. Thus, for the purposes of making such comparisons, we have rescaled the estimates of percent increases in daily deaths using an increase in levels of particles of 100 $\mu g/m^3$.

For the few studies in which COH was used (Schimmel and Murawski 1976; Mazumdar and Sussman 1983; Fairley 1990; Kinney and Özkaynak 1991), our results are qualitatively similar. Table 31 reveals that our estimates for TSP are similar to those reported in other studies. For $PM_{2.5}$ and PM_{10}, our estimates are also consistent but tend to fall in the lower range of results, but predicted $PM_{2.5}$ is more in accord with published figures.

In few time-series studies have cause-specific mortality been examined. Our results for cancer, cardiovascular, and respiratory deaths for TSP and PM_{10} (lag 0) fall within the observed range (Table 32). In addition, our results are similar to those found in time series analyses of the cities included in the Harvard Six Cities Study, in which Schwartz and colleagues (1996) measuring PM_{10} found an 18.4% increase in the daily number of deaths (Table 33) as compared to our results of 25.3% increase (using the 3-day mean for predicted $PM_{2.5}$, Table 31). Because few studies have compared two or more age groups as we did, it is difficult to make comparisons (Table 33).

Although we did not find an association at the 3-day mean for subjects with nonmalignant digestive diseases, the daily number of deaths from this cause increased with levels of particles evaluated at lag 0. While this result is unusual and could well be due to chance, it is not unprecedented in that positive associations between daily deaths from digestive diseases and black smoke (but not for SO_2) were found in two Polish cities (Cracow and Poznan), but not in two other cities (Lodz or Wroclaw) (Wojtyniak and Piekarski 1996).

In analyzing results for sulfate, we found that the percent increase in nonaccidental deaths, scaled again to a per 100 $\mu g/m^3$ increase, were (at lag 0) 32.7% for Sutton sulfate and 48.3% for predicted sulfate measured from $PM_{2.5}$. For deaths from cardiovascular conditions our estimates were 17.8% and 23.8%, respectively, and for deaths from respiratory conditions the respective estimates were 41.4% and 81.9%. These results are similar to those of Schwartz and coworkers (1996) who noted an overall increase of 24.5% in daily mortality for the cities that comprised the Harvard Six Cities cohort study. As well, our results are in close agreement with hospital admission data in Ontario, for which Burnett and colleagues (1995) found a 32.2% increase for respiratory admissions and a 23.7% increase for cardiac admissions. Burnett and colleagues (1998) also found that a 100 $\mu g/m^3$ increase in sulfate was associated with a 21% increase in daily nonaccidental mortality in Toronto over the 15-year period 1980 to 1994.

ANALYSES BY INDICATORS OF DISEASE GROUP BEFORE DEATH

We found statistically significant positive associations across most indices of PM among individuals who, shortly before death, were classified as having cancer, acute lower respiratory diseases, cardiovascular diseases, chronic coronary artery disease (especially in the ≥ 65 group), and congestive heart failure. The strongest association was found with congestive heart failure. No consistent associations were found for acute or chronic upper respiratory diseases, definite airways disease, acute coronary artery disease, hypertension, and cerebrovascular diseases. Table 34 provides a summary of these results for an increase of predicted $PM_{2.5}$ of 100 $\mu g/m^3$ and contrasts these results with those of the analyses of cause-specific mortality.

In the analyses in which the indices representing persons with cardiovascular diseases, lower respiratory conditions,

Table 31. Percentage Increases in Daily Nonaccidental Deaths in Relation to 100 μg/m^3 Increases for TSP, PM_{10}, and $PM_{2.5}$ Between Present Investigation and Selected Other Studies

Source	TSP (%)	PM_{10} (%)	$PM_{2.5}$ (%)
Montreal (Present Study)[a]			
lag 0	6.7	6.9	6.3
lag 1	3.7	3.8	12.2
Predicted $PM_{2.5}$, lag 0			21.4
Predicted $PM_{2.5}$, lag 1			16.7
Predicted $PM_{2.5}$, 3-day mean			25.3
North and South American Studies			
Birmingham (Schwartz 1993; Samet et al 1995)		10.7–11.0	
Cincinnati (Schwartz 1994b)	6.0		
Cook County, Illinois (Ito and Thurston 1996)		5.0	
Cook County, Illinois; ≥ 65 years (Styer et al 1995)		5.5	
Detroit (Schwartz 1991)	6.0		
Eastern Tennessee (Dockery et al 1992; Samet et al 1995)		17.4	26.0
Harvard Six Cities, mean (Schwartz et al 1996a)		8.3	16.1
Los Angeles (Kinney et al 1995)		5.0	
Mexico City (Borja-Aburto et al 1997)	2.0–6.0		
Minneapolis (Schwartz 1994a)	5.0		
Philadelphia (Moolgavkar et al 1995)	1.6		
Philadelphia (Samet et al 1995)[b]	2.7–8.6		
Philadelphia (Schwartz and Dockery 1992)	7.0		
Salt Lake County, Utah; ≥ 65 years (Styer et al 1995)		0.0	
Utah Valley (Pope et al 1992; Samet et al 1995)		16.0–17.4	
Santiago, Chile (Ostro et al 1996)		8.0	
São Paulo, Brazil (Saldiva et al 1995)		13.0	
St Louis (Dockery et al 1992; Samet et al 1995)		16.2	19.0
Steubenville (Moolgavkar et al 1995)	2.0		
Steubenville (Schwartz and Dockery 1992)	4.0		
European Studies			
Amsterdam, The Netherlands (Verhoeff et al 1996)		2.3–6.2	
Athens, Greece (Touloumi et al 1996)[c]		5.0	
Barcelona, Spain (Sunyer et al 1996)[c]		7.0	
Bratislava, Czech Republic (Bacharova et al 1996)	0.0		
Bratislava, Czech Republic (Bacharova et al 1996)	1.0		
East Berlin, Germany (Rahlenbeck et al 1996)[d]	4.6–6.2		
Köln, Germany (Spix and Wichmann 1996)	5.0–6.9		
London, England (Anderson et al 1996a)[c]		12.8–21.8	
Lyon, France (Zmirou et al 1996)[e]		2.0	
Rome, Italy (Michelozzi et al 1998)[d]	3.9		
Valencia, Spain (Ballester et al 1996, 1997)[c]		9.4	

[a] These data are unadjusted for gaseous pollutants.

[b] Various models, not accounting for season.

[c] Assuming black smoke approximately equivalent to PM_{10} (Dockery and Pope 1994; Muir and Laxen 1995).

[d] Assuming suspended particles approximately equivalent to TSP.

[e] Assuming $PM_{13} \sim PM_{10}$.

and cancer were combined into mutually exclusive groups, we found increases in daily mortality for persons who were not attributed as having any of these conditions, to persons with cardiovascular disease and cancer, and to persons with cardiovascular disease and lower respiratory diseases.

Table 32. Percentage Increases in Daily Number of Deaths from Cancer, Respiratory, and Cardiovascular Causes in Relation to Increases of 100 μg/m^3 for TSP and PM_{10} Between Present Investigation (Unadjusted for Gaseous Pollutants) and Selected Other Studies

Disease	TSP (%)	PM_{10} (%)
Cancer		
Montreal (Present study)–lag 0	5.5	6.9
Montreal (Present study)–lag 1	–0.9	–13.2
Cook County, Illinois (Ito and Thurston 1996)		12.0
Philadelphia (Schwartz and Dockery 1992)	4.0	
Cardiovascular Diseases		
Montreal (Present study)–lag 0	6.7	7.4
Montreal (Present study)–lag 1	–0.9	9.4
Barcelona (Sunyer et al 1996)[a]		9.3
Birmingham (Schwartz 1993)		17.0
Bratislava (Bacharova et al 1996)	1.0	
Cincinnati (Schwartz 1994b)	8.0	
Cook County, Illinois (Ito and Thurston 1996)		3.0
London (Anderson et al 1996a)[a]		4.2
Lyon (Zmirou et al 1996)[b]		8.0
Philadelphia (Schwartz and Dockery 1992)	10.0	
Rome (Michelozzi et al 1998)[c]	3.8	
Santiago (Ostro et al 1996)		7.9
Utah Valley (Pope et al 1992)		43.0
Valencia (Ballester et al 1996, 1997)[a]		13.1
Respiratory Diseases		
Montreal (Present study)–lag 0	5.8	16.54
Montreal (Present study)–lag 1	13.5	7.2
Barcelona (Sunyer et al 1996)[a]		9.7
Cook County, Illinois (Ito and Thurston 1996)		14.0
London (Anderson et al 1996a)[a]		4.8
Lyon (Zmirou et al 1996)[b]		8.0
Milan (Vigotti et al 1996)	12.0	
Paris (Dab et al 1996)[a]		17.0
Rome (Michelozzi et al 1998)[c]	2.9	
Santiago (Ostro et al 1996)		14.0
Utah Valley (Pope et al 1992)		20.0
Valencia, Spain (Ballester et al 1996, 1997)[a]		0.9

[a] Assuming black smoke approximately equivalent to PM_{10} (Dockery and Pope 1994; Muir and Laxen 1995).

[b] Assuming $PM_{13} \sim PM_{10}$.

[c] Assuming suspended particles approximately equivalent to TSP.

METHODOLOGIC ASPECTS

Mortality Data

We assumed that the underlying causes of death were coded accurately or that these inaccuracies had constant probability distributions over the ten-year period that this study was carried out. There are no reports regarding 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). Cancer is usually coded 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, errors may arise in selecting one underlying cause in a complex chain of health events (eg, cancer leading to pneumonia and then to respiratory failure).

Table 33. Percentage Increases in Daily Nonaccidental Deaths According to Age in Relation to Increases of 100 μg/m^3 for TSP and PM_{10} Between Present Investigation (Unadjusted for Gaseous Pollutants) and Selected Other Studies

Age	TSP (%)	PM_{10} (%)
< 65 Years		
Montreal (Present study)–lag 0	5.7	18.4
Montreal (Present study)–lag 1	–9.9	–8.8
Philadelphia (Schwartz and Dockery 1992)	2.7	
≥ 65 Years		
Montreal (Present study)–lag 0	7.1	3.7
Montreal (Present study)–lag 1	8.2	8.0
Barcelona; > 70 years (Sunyer et al 1996)[a]		6.3
Harvard Six Cities, mean (Schwartz et al 1996)		18.4[c]
Philadelphia (Schwartz and Dockery 1992)	9.5	
Rome (Michelozzi et al 1998)[b]	4.3	
Salt Lake County (Styer et al 1995)		0.0
Santiago (Ostro et al 1996)		11.0
São Paulo (Saldiva et al 1995)		13.0
Valencia; > 70 years (Ballester et al 1996, 1997)[a]		8.7

[a] Assuming black smoke approximately equivalent to PM_{10} (Dockery and Pope 1994; Muir and Laxen 1995).

[b] Assuming suspended particles approximately equivalent to TSP.

[c] Results for $PM_{2.5}$.

Table 34. Mean Percent Increase Between Daily Cause-Specific Mortality and Daily Mortality for Groups with Selected Health Conditions Before Death, for Increase Equal to 100 μg/m^3 in Predicted $PM_{2.5}$, by Lag Period[a]

	Lag 0		3-Day Mean	
Endpoint	Underlying Cause of Death	Disease Group	Underlying Cause of Death	Disease Group
Nonaccidental Deaths	21.4[b]		25.4[b]	
< 65 years	21.0[b]		11.4	
≥ 65 years	22.0[b]		32.1[b]	
Neoplasms	17.6[b]	19.7[b]	15.8	21.2[b]
< 65 years	12.4	15.2	5.5	10.8
≥ 65 years	19.9[b]	21.7[b]	20.7	25.9[b]
Cardiovascular Diseases	10.7	23.8[b]	14.7	33.2[b]
< 65 years	9.0	47.3[b]	5.8	14.4
≥ 65 years	11.3	18.4[b]	15.9	35.2[b]
Coronary Artery Disease	11.5	19.9[b]	19.2	21.3[b]
< 65 years	8.4	43.3	17.0	−4.2
≥ 65 years	11.6	15.9	19.9	27.6[b]
Congestive Heart Failure		42.8[b]		51.4[b]
≥ 65 years		47.3[b]		54.8[b]
Respiratory Diseases	44.8[b]		119.0[b]	
≥ 65 years	54.8[b]		148.4[b]	
Acute Lower Respiratory Disease		24.7[b]		62.5[b]
< 65 years		32.1		56.6
≥ 65 years		21.3		62.7[b]
Airways Disease		16.6[b]		14.9
< 65 years		26.4		29.3
≥ 65 years		14.7		11.9

[a] Blank entries mean data not analyzed.

[b] Corrected *t* value > 1.96.

Our comparison between the underlying causes of death and groups of cancer, respiratory conditions, and cardiovascular diseases was consistent with these general observations (Table F.13).

Confounding Variables

Only variables that are associated with both mortality and air pollution can confound the association (Breslow and Day 1980). However, in time-series analyses, an additional constraint exists: that only those factors that vary in time over a period of days or weeks can confound the observed associations (Dockery and Pope 1994). Thus, smoking and alcohol consumption are unlikely to confound associations in the ten-year period of this study, but weather and infectious disease epidemics might be important confounding variables.

Weather is associated with both daily mortality and air pollution. We selected weather variables that minimized the residual variability in the mortality time series (minimum AIC), after accounting for annual, seasonal, and subseasonal patterns. The strategy used to select weather variables had the advantage of being based on clear-cut and reproducible criteria and was also driven by statistical considerations. An alternative strategy of including weather variables that are known to be causally associated with mortality could not be undertaken as there are no such data for Montreal. (Of course, extremely hot and humid conditions are known to increase mortality [Katsouyanni et al 1993; Ballester et al 1997].) We are unaware

of any theoretical models or empirical results that would indicate which lag structure should be used (eg, specific lags, averages, or an index to indicate consecutive days of extreme weather conditions).

The population of Montreal is subject to seasonal variations in temperature and humidity. All homes in Montreal have heating and most are reasonably well insulated so that few persons suffer badly from the cold. As well, the social assistance support available in Canada protects individuals from the extremes of winter weather. In the summer, short periods of hot and humid conditions occur, but temperatures are far below those experienced in the central and southern United States. Thus, in view of the sociodemographics and weather patterns in Montreal, it seems reasonable to believe that weather is not a strong confounding factor. These arguments are consistent with the data, for which we observed that the effects of particles were rather insensitive to the range of weather models considered, implying that little residual confounding resulted from fluctuations in weather. These observations are consistent with those of Samet and colleagues (1998) who considered a wide variety of options to control for weather.

We adjusted for the effects of other gaseous pollutants. Many of these pollutants are generated from complex chemical reactions in air. For example, the gaseous pollutants (NO_2 and SO_2) act as precursors in the formation of particles. These atmospheric chemical processes create high correlations among levels of most pollutants. In addition, the same sources generate many pollutants, so that including these other chemical species in the statistical models may lead to an overadjustment for the effects of particles. In addition, these correlations may lead to statistical difficulties in simultaneously adjusting for many of these variables, in that the models may have been overfitted. This may be particularly relevant for the time series that were based on infrequent observations or small numbers of deaths.

While we noted differences in the estimates after we adjusted for the gaseous pollutants, our conclusions would not be greatly altered from those resulting from the models that did not contain these pollutants. These conclusions may be tempered in that, unlike the analyses of weather factors, we only adjusted for the effect of pollutants as measured on the concurrent day, regardless of the day in which exposure to particles was being assessed. It is conceivable that we could have arrived at different results had the models been altered to consider different lag structures for gaseous pollutants.

Finally, we could not control for the effects of infectious disease epidemics (eg, influenza, which occurs mostly in the fall and winter, when particle levels are increased) because no databases that could be used for this purpose exist. Because these epidemics generally follow seasonal and subseasonal weather patterns, as mentioned above, it is likely that some or all of the confounding effects were removed during the temporal filtering. However, it remains possible that the associations between PM and mortality may have been confounded. In a few studies, adjustment for influenza epidemics did not remove associations between mortality and suspended particles or SO_2 (Spix et al 1993; Anderson et al 1996b; Vigotti et al 1996).

Components of Ambient Particles

This study used outdoor levels of air pollution at fixed-site monitoring stations, averaged across the various monitoring stations in the city, and no account was made for variations within the city. However, correlations in exposure levels between monitors and the results from our Montreal study of variations in TSP and PM_{10}, suggested that taking averages was not likely to bias the results appreciably.

COH is similar to the soiling index or British smoke that have been used in other countries. The measurements are made by drawing air through a filter paper and collecting particles for an hour. The size of the particles collected is not carefully controlled, but it is likely that it is biased toward smaller particles (< 10 μm or even < 2.5 μm). COH is more sensitive to particles that will reduce the light signal (ie, light absorbing). There are differences among the airborne particles with respect to their light absorbing characteristics and, thus, COH will tend to measure black carbon or elemental carbon. Key sources of elemental carbon are diesel emissions, inefficient combustion processes such as wood burning, and some industrial processes. However, most combustion processes, particularly high temperature combustion, have the potential to produce elemental carbon. Despite the infrequent use of COH in time-series analyses, our data show it to be a reliable measure of the concentration of carbon particles in the air, with only limited contributions from other pollutants, such as sulfate, nitrates, or particle mass. By using this index, as well as the other measures of particle mass and sulfate, we gained additional information regarding the effects of air pollution on human health that is not normally available to investigators.

We found considerable spatial variability across the study area for both particle and gaseous measures (Table 7). Sulfate was only slightly variable, but TSP had more variability with a few locations showing high, but explainable elevations in concentrations (at intersections of highways and near a municipal solid waste landfill site). We expected a higher intersite correlation for COH than we

observed, and this could be due to measurement errors or to actual spatial variations in carbon (from automobile exhaust, for example, where both mean levels of COH and TSP were much higher at the junctions of major expressways). The only measures that were spatially homogeneous were $PM_{2.5}$ and sulfate (correlation of about 0.9 between Montreal and the Sutton station). Averaging data across monitors would smooth out local scale variations but would measure prevailing background levels, thus producing a reasonable and likely unbiased population mean exposure.

For spatially heterogeneous measures, use of exposure values from monitors close to subjects' residences would not improve our estimates because we have no information regarding mobility patterns, so this type of assignment would introduce yet another level of misclassification into what is already an imperfect process.

For subjects who were not mobile (eg, hospitalized at time of death), it would have been conceivable to improve the exposure assessment using spatially proximal monitors, which require separate analyses for each exposure group. Such an analysis is not likely to be very informative: statistical power is lost because the number of subjects with any condition could be distributed among the 18 major hospitals and numerous minor ones in Montreal.

Measurements of total sulfate at the Sutton monitoring station were used as surrogates for sulfate in Montreal. The Pearson correlation coefficient between the Sutton station and the two monitoring stations in Montreal measuring sulfate from $PM_{2.5}$ was very high (about 0.9). Thus, these measurements identified background levels that were relatively homogeneous on large distance scales but were likely to be somewhat misclassified as they did not capture local fluctuations. Statistical power in the analyses of Sutton sulfate was reduced because only eight of ten years of measurements were available.

We estimated mean daily TSP and COH using measurements from all fixed-site monitors in the city. As we showed, levels of these two pollutants were higher near the major highways that course through the city (this was not true for sulfate and $PM_{2.5}$), so that there is an argument for excluding these monitors from the averages to be used in the analyses. We did not attempt analyses excluding monitors near the highway in this study, but such evaluations could be conducted as sensitivity analyses at a later date.

We had considerably reduced statistical power for the analyses of TSP and $PM_{2.5}$ and PM_{10}, because only about 600 days of measurements were available. Although we found high values of R^2 for the two predicted time series ($PM_{2.5}$ and sulfate from $PM_{2.5}$), these two predicted time series were likely more misclassified than the original ones. However, the results were consistent with other measures of particles that we used and provide, at the very least, more statistical power than did the incomplete fine particle series.

We conducted analyses using three different lags: 0-day lag, 1-day lag, and 3-day mean. The restricted set of lag periods should have provided a reasonably good picture of the short-term effects of the pollutants under investigation. We know of no data or theoretical models that could be used to determine which lag structure is the more appropriate. Intuitively, however, it seems that increased daily mortality should be found when exposures are higher over a period of a few days than a single day, and this is what we found generally. An alternative interpretation of this lag structure is that the particle effects are time distributed: some people die on the day of exposure while others die one or two days after exposure.

In addition to the substances that were measured routinely, other chemicals are in outdoor air (eg, volatile organic compounds). As we did not have daily measurements of these and other compounds, it was not possible to account for their effects.

Our estimates of the effect of sulfate obtained from TSP were likely to be attenuated because sulfate from TSP would have an SO_2 artifact (arising from the absorption of SO_2 onto glass-fiber filters). In our Toronto mortality study (Burnett et al 1998), we reported that the slope of the regression line between sulfate from high-volume samplers using glass fiber filters and sulfate from the dichotomous monitors that use teflon filters was 0.87. The correction to our data would thus be to multiply the regression coefficient for sulfate from TSP by 1.1494.

In this, as in other time-series studies of air pollution, the estimates of percent increases in daily mortality for ambient pollution excluded by necessity particles and other pollutants from indoor sources. The study design assumed that total personal exposure to particulates can be partitioned into two components: outdoor and indoor sources. Two unanswered questions, then, are whether this assumption is correct and whether the effects observed in this and other studies were confounded by indoor air pollution.

With regard to the first question, fine and ultrafine particles penetrate indoors (Dockery and Spengler 1981a,b; Spengler et al 1981; Spengler and Sexton 1983), and individuals will be exposed to these ambient particles regardless of their activity patterns (unless their indoor air is filtered). For example, Dockery and Spengler (1981a,b) estimated that the infiltration of fine particles into indoor structures is about 70%, although a fully air conditioned building could reduce this to about 30%.

North Americans spend almost 88.6% of their time indoors (6.1% outdoors and 5.3% in vehicles) (Leech et al 1996), and this figure may be higher in the winter months, so one would expect indoor air to be important in these time-series studies. The component of particle pollution due to indoor sources will vary by individual, depending on specific activity patterns. The main argument for partitioning the two components of particles is that the type of particles generated indoors will be different from ambient air particles: outdoor particles consist of coarse particles from dust, and finer fractions of sulfate, nitrates, and carbon particles generated mostly from internal combustion, whereas indoor air particles are generated from cigarette smoke, radon, indoor combustion of fuels, molds, fungi, indoor activities, shedding of human skin, and personal grooming habits (Spengler and Sexton 1983; Wallace 1996). Should these levels remain approximately constant on short time scales (eg, from smoking, which on a population level does not vary appreciably from day to day), then the effect on daily mortality will be minimal and the indoor component should not confound the effects of the outdoor component. While most cross-sectional studies have found very low correlations between personal levels and indoor and outdoor levels (eg, Dockery and Spengler 1981b; Wallace 1996), a recent within-subject study suggested much higher correlations than in previous research (Janssen et al 1998). In time-series studies, it is the longitudinal component of variability that is of concern and not the cross-sectional one.

Measurement error introduced by using fixed-site monitors and excluding other internal sources of particles which are comparable in terms of their toxicological potency should bias associations toward the null hypothesis of no effect (Zidek et al 1996). The main effect of this misclassification is to underestimate the magnitude of the effect and to decrease statistical precision. To interpret analyses of cause-specific mortality is difficult because of the larger statistical noise inherent in these smaller time series as well as errors in classifying causes of death. Zeger and colleagues (2000) have pointed out that "the generic criticism—that measurement errors render the results of such time-series models uninterpretable—is incorrect," although errors may still exist from selection or confounding bias that have hitherto gone unrecognized (Goldberg 1996).

Another important issue is whether one or more agents can be identified from the complex mixture of air pollutants. This problem is analogous to identifying the toxic components of tobacco smoke, which contains thousands of chemicals. Unlike tobacco smoke, however, we are able to routinely measure most of the different components of the air pollution mixture and relate levels directly to health outcomes. However, the interpretation of estimates of effect for any one pollutant is clouded because of strong correlations between pollutants, even after accounting statistically for other pollutants in the analyses. We have not yet investigated the synergistic effects that depend on the complex mixture of pollutants.

Morbidity Data

The data used to construct the indices of disease group consisted of health care billing data, diagnostic codes recorded on the billing record, rendered health care services (only recording the fact that a procedure was carried out, with no results recorded), and filled prescriptions for drugs that were paid for by the QHIP. These billing data reflect underlying health status over long periods of time because they provide clinical information about QHIP participants both within and outside the hospital. The fact that pharmaceuticals are not covered during hospital stays should not have limited our defining morbidity status because we probably identified the most important prescriptions that could define disease group when subjects were out of the hospital. Thus, the QHIP data should in principle perform more accurately than simple hospital discharge summaries, which provide, at best, a snapshot of acute illnesses.

The key assumption in using the QHIP data was that they were sufficiently accurate to define most conditions before death. In defining our indices, we assumed that certain conditions could not be identified accurately. As a result, we grouped related conditions together into specific rubrics; for example, we defined airways disease but did not attempt to identify its individual components (eg, asthma).

An essential element in defining the indices of disease group was the diagnosis recorded on the billing record. Although this was available for only about 50% of the billing records, well over 96.5% of deceased subjects had at least one diagnosis coded in the five-year period before death. We are aware of no data regarding the accuracy of these diagnoses, and it is likely that accuracy depends on the disease, the specialty of the physician, and other characteristics of physicians and subjects. For example, diagnoses for cancer and stroke should have been accurate because of well-established investigative procedures used by specialists, whereas the accuracy of diagnosing asthma would be problematic because appropriate tests would not be conducted by all physicians.

The next most important indicator was records of filled prescriptions. Although we had no information regarding compliance for taking drugs, this may be irrelevant in the context of defining groups because we were only interested

in whether a prescription indicated the presence of a specific health condition. We also had no information regarding prescriptions that were written by physicians but never filled by subjects; this kind of missing information will inevitably lead to misclassification that may vary by disease and socioeconomic status. In addition, administrative changes to the QHIP system have led to dramatic changes in drug usage. Specifically, as an incentive to reduce unnecessary medication, a $2 charge to seniors was instituted in 1992. As a result, usage dropped dramatically for both critical and less-necessary drugs. For example, the percentage of deceased subjects taking medications for coronary artery disease and congestive heart failure fell by 6% from the previous year. In the final year of the study, this modification in Quebec's drug plan may have led to some misclassification of subjects in morbidity groups that relied on drug data.

The drug plan covered persons who were ≥ 65 years. Therefore, limited drug prescription data were available for persons who died exactly at age 65. To carry out analyses excluding persons who died at 65 would have been useful, but this was not possible because the QHIP provided us only with five-year age groups (for reasons of confidentiality). Thus, it is likely that some inaccuracies occurred in classifying subjects into groups that were based on prescriptions.

We were unable to follow the natural history of disease for each subject. We thus arbitrarily defined three time periods before death (two months, six months, one year) and used the two-month interval to capture acute conditions and the one-year period to capture chronic conditions. By this decision, we attempted in a qualitative manner to trade off specificity and sensitivity, accounting for the inconsistent manner in which clinicians recorded information in the billing databases. The data for chronic disease clearly showed a substantial loss of information if too short a time period was used. On the other hand, the two-month period for acute diseases seemed justified, although it resulted in rather sparse time series of deaths.

The indicators of disease group for the cardiovascular diseases and respiratory conditions were defined by two specialists with considerable clinical and research experience who are familiar with the Quebec health care system. These indices were complex and required appropriate expertise to define. The rationale for our judgments about defining the indices was based on our knowledge of clinical practice in Quebec, the effective lack of standardization of medical practice, and the information required to provide an adequately accurate diagnosis.

For example, the requirement of having three diagnoses on the billing record to define hypertension was based on usual clinical practice guidelines. However, these diagnoses were surrogates for actual tests with positive results. Misclassification can occur if the tests were not actually conducted (which seems unlikely for hypertension, because blood pressure measurement is a simple, routine test), or if the physician did not in fact record a diagnosis of hypertension after each positive test. In addition, it is possible that not all physicians use the same definition for defining hypertension (usually defined as ≥ 140 mm Hg systolic and ≥ 90 mm Hg diastolic blood pressure), and these definitions may vary by characteristics of both the subjects and the physician. On the other hand, our use of pharmaceutical data in the elderly almost guarantees that we have the potential to identify all treated cases. Over 70% of deceased elderly subjects with hypertension had a prescription for antihypertensive pharmaceuticals in the year before their death. It is also possible that subjects who did not fill their prescriptions for treatment of hypertension may have been excluded, although we are not aware of any data that indicate the extent of this problem.

As an indicator of the accuracy of our disease groups, for example, we could compare the prevalence of hypertension to that obtained from specially designed surveys. Using our definitions, we estimated that the one-year period prevalence of hypertension among the elderly was 7% and the estimated five-year period prevalence was 20%. In comparison, the self-reported estimate of the prevalence of hypertension (defined as ≥ 140 mm Hg systolic and ≥ 90 mm Hg diastolic blood pressure) as diagnosed by a physician was 9% (Heart and Stroke Foundation of Canada 1999). Thus, our five-year estimate of prevalence using the QHIP data was similar to estimates in this population-based health survey of Canadians. We therefore interpret our one-year estimate as reflecting the point prevalence of treated hypertension.

The use of fixed time periods may have also affected the accuracy of defining these indices. Again, for hypertension, to use a cutoff of one year before death may have led to the exclusion of subjects who had one or more diagnoses before one year, unless they had a filled prescription during that time interval. On the other hand, it would be unlikely that having a prescription for hypertension drugs before the one-year cutoff would lead to a false negative because the average duration of prescriptions is 30 days.

We therefore believe that both the sensitivity and specificity for defining the health status indicators were probably relatively high; however, substudies investigating the accuracy of these definitions would be useful.

The cancer index, defined by the first author of this report, was much simpler to define than the respiratory and cardiovascular indices, because it was only necessary

to list the appropriate ICD-9 codes, neoplastic drug class, and surgical procedures. Because we could not use radiotherapeutic billing codes, some subjects with cancer may have been inadvertently excluded, although it is likely that this number was relatively small.

A major advantage of using morbidity data to define disease group was that groups of subjects could be combined into mutually exclusive categories. This combining could not be achieved by using data on underlying causes of death. The analyses presented in this report should be considered preliminary, in that we only combined three major groups (lower respiratory, cardiovascular, and cancer). The evaluations of groups suggested that more specific analyses should be considered that combine groups such as acute lower respiratory diseases, chronic coronary artery disease (especially in the elderly), and congestive heart failure.

Because the study focused on a set of a priori conditions, we did not investigate other conditions. Indeed, we found an association for persons who did not have any of the three main conditions, suggesting that other groups we did not analyze may well be at higher risk. The largest constituents of this group were persons with diabetes (based on ICD-9 codes recorded on the billing record), anemias, organic psychotic conditions, cardiac dysrhythmias, atherosclerosis, gastrointestinal diseases, and cardiovascular symptoms. The fact that we found an association between particles and daily mortality from diabetes (using underlying cause of death), and that diabetes is a large constituent of this group, implies that further analyses of certain groups are warranted. (Indeed, using diagnostic codes from the QHIP billing database [one year from death], we found that 63.3% of these deaths had at least one ICD-9 code attributed to diabetes [ICD-9 250].)

STATISTICAL POWER AND MULTIPLE TESTING

For the particle time series that were complete, we had sufficient statistical power to detect increases in daily mortality for the most important causes of death (all nonaccidental deaths, cancer, and cardiovascular). For the less frequent causes of death, statistical power was reduced. Age group comparisons were severely compromised by the few numbers of deaths before age 65, but the data indicate increased daily mortality associated with particles in persons ≥ 65 years.

The issue of multiple comparisons has a bearing in interpreting the results of this study because many associations have been investigated simultaneously. Thus, some statistically significant results may have occurred by chance. However, following the current consensus among epidemiologists, we did not formally correct *p* values or CIs for the number of comparisons made (Thomas et al 1985; Marshall 1990; Rothman 1990). False-positive associations are best distinguished from true associations by minimizing potential biases in the study, careful examination of the data, consideration of arguments of plausibility, comparison with previous investigations, and by testing in future studies.

The consistency of our findings for some underlying causes of death compared with previous investigations suggests that there may be few spurious findings in the present study, although the new findings need to be corroborated in other investigations. While we are somewhat skeptical about the association for nonmalignant digestive diseases, because of inconsistency between exposure measurements, it was interesting to find associations for diabetes, cancer, and those persons who did not have cardiovascular diseases, or lower respiratory diseases, or cancer. Frank and Tankersley (1997) suggested that persons whose health is failing may be at increased risk.

The positive associations found for persons with acute lower respiratory diseases and congestive heart failure as well as for those who had both cardiovascular diseases and lower respiratory diseases before death are consistent with the hypothesis of Bates (1992), who suggested that exposure to air pollutants in persons who had cardiac disease with myocardial damage may cause acute pulmonary disease, such as bronchiolitis or pneumonia, thereby leading to congestive heart failure. However, our failure to find an association with acute coronary artery disease is not consistent with the hypothesis of Seaton and collaborators (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.

IMPLICATIONS OF THIS RESEARCH

Data from this study can be used directly to inform both science and the development of air quality standards. An important caveat is that this is the only time-series study to date to investigate potentially vulnerable groups using medical information before death, so care must be taken in generalizing the results. Although we believe that the data are valid and should be representative of most countries in which universal health care systems operate, the relatively small sizes of some groups, the definitions used for these groups, and undetected biases make it crucial that our study be replicated in other locations. The toxicology community can use these data to develop appropriate models to further investigate these groups and thus shed light on specific mechanisms. Moreover, as exposure limits should

be driven by the most susceptible populations, this research can be used directly to inform specifically on the development of new regulations.

As explained above, we observed higher excess daily mortality in a number of groups, and excess daily mortality in some of these groups was higher than that found for all nonaccidental deaths. In Table 35 we compare the MPC in daily mortality for a 100 $\mu g/m^3$ increase in air pollution, evaluated at the 3-day mean for selected groups, relative to the mean increase in daily nonaccidental mortality. Of the groups that showed statistically significant increases in daily mortality, acute lower respiratory disease and congestive heart failure had daily increases that were more than twice that found for nonaccidental deaths. When we complete our investigation of combinations of conditions, it may reveal other groups with even higher relative excess daily mortality.

Table 35. Ratio of Effects for Selected Disease Groups in Relation to That Obtained for Daily Nonaccidental Mortality, for an Increase of 100 $\mu g/m^3$ Evaluated at the 3-Day Mean for Predicted $PM_{2.5}$ and Total Sulfate from the Sutton Station

	Relative Increase in the Mean Percent Change in Daily Mortality of Groups with Respect to Mean Increase in Daily Nonaccidental Mortality	
Disease Group	Predicted $PM_{2.5}$	Sutton Sulfate
Cancer	0.83	0.63
Respiratory Disease		
Acute lower respiratory disease	2.46	2.14
Airways disease	0.59	0.34
Cardiovascular Disease		
Acute coronary artery disease	1.05	0.72
Chronic coronary artery disease	1.01	0.43
Congestive heart failure	2.03	1.69
Any coronary artery disease	0.84	0.47
Any cardiovascular disease	1.31	0.87

FURTHER RESEARCH

We believe that we have only scratched the surface of this extensive database. With the proliferation of groups and the multiple indices for particles, a multilevel analysis, such as empirical Bayes, may be useful. The results of the combined group analyses suggest that other groups should be created (eg, diabetes) from the one in which persons had neither cardiovascular diseases, respiratory conditions, nor cancer. Developing substudies to investigate the sensitivity and specificity of the indices used to define health states would be useful. In addition, it is important to investigate more precise combinations of conditions than in the present study in order to establish accurately which subpopulations are the most frail. Although this report focused on ambient particles, we found a clear signal for the many gaseous pollutants considered. A detailed analysis of these pollutants will provide a more complete picture to this emerging story of who may be susceptible to the effects of air pollution.

The adverse health effects that we have observed may be due to the mixture of particles and gaseous pollutants. Stronger evidence to support PM effects over gaseous effects may be due to differential errors in measurement (PM ambient monitors are better predictors of population average exposure than gas monitors) and issues related to mixtures (PM is part of the complex mixture of aerosols). In the present study, PM effects were compared to the effects of each gas separately. Temporally and geographically consistent results may be observed if the combined effects of gases were compared to PM mass effects. Latent variable analyses may be appropriate within this context.

ACKNOWLEDGMENTS

The authors gratefully acknowledge of the assistance of Jacques Barry, Holly Lam, Marie-Claude Boivin, David Johnson, and Claude Gagnon. We also appreciate the assistance, support, and thoughtful suggestions of Drs Frank Speizer, Jonathan Samet, Aaron Cohen, and Diane Mundt during the course of the investigation. We thank the Montreal Urban Community and Environment Canada for providing the NAPS, CAPMoN, CAAMP, and weather data and we are grateful to the Ministère de la santé et des services sociaux de Québec for providing the health data. Dr Goldberg and Dr Tamblyn gratefully acknowledge receipt of separate National Health Scholar awards from the National Health and Research Development Program of Health Canada, and Dr Goldberg acknowledges support from the Fonds de la Recherche en Santé du Québec.

REFERENCES

Abbey DE, Lebowitz MD, Mills PK, Beeson WL, Petersen F, Burchette RJ. 1995. Long-term ambient concentrations of particles and oxidants and development of chronic disease in a cohort of nonsmoking California residents. Inhalation Toxicol 7:19–34.

Abbey DE, Mills PK, Petersen FF, Beeson WL. 1991. Long-term ambient concentrations of total suspended particulates and oxidants as related to incidence of chronic disease in California Seventh-Day Adventists. Environ Health Perspect 94:43–50.

Abbey DE, Petersen F, Mills PK, Kittle L. 1993. Chronic respiratory disease associated with long-term ambient concentrations of sulfate and other air pollutants. J Expos Anal Environ Epidemiol 3:99–115.

Abbey DE, Nishino N, McDonnell WF, Burchette RJ, Knutsen SF, Lawrence B W, Yang JX. 1999. Long-term inhalable particles and other air pollutants related to mortality in nonsmokers. Am J Respir Crit Care Med 159:373–382.

Acquavella JF, Donaleski D, Hanis NM. 1986. An analysis of mortality follow-up through the national death index for a cohort of refinery and petrochemical workers. Am J Ind Med 9:181–187.

Adams B, Boyum J, Griffin G, Ypshida C. 1995. Oakridge, Oregon, 1994 PM_{10} Saturation Monitoring Study. Monitoring and Data Analysis Section Report, US Environmental Protection Agency Region 10 Supplemental Grant.

Alderson MR, Meade TW. 1967. Accuracy of diagnosis on death certificates compared with that in hospital records. Br J Prev Soc Med 21:22–29.

Anderson HR, Ponce de Leon A, Bland JM, Bower JS, Strachan DP. 1996a. Air pollution and daily mortality in London: 1987–92. Br Med J 312:665–669.

Anderson HR, Atkinson R, Limb ES, Strachan DP. 1996b. Asthma epidemics and air pollution. Epidemic of asthma was not associated with episode of air pollution (letter). Br Med J 312:1606–1607.

Anonymous. 1993. PM_{10} saturation monitoring study conducted in Ashland, Kentucky. Amtic News, 2, pp 2–5.

Bacharova L, Fandakova K, Bratinka J, Budinska M, Bachar J, Gud-aba M. 1996. The association between air pollution and the daily number of deaths: Findings from the Slovak Republic contribution to the APHEA project. J Epidemiol Community Health (Suppl 1) 50:S19–21.

Ballester F, Corella D, Perez-Hoyos S, Hervas A. 1996. Air pollution and mortality in Valencia, Spain: A study using the APHEA methodology. J Epidemiol Community Health 50:527–533.

Ballester F, Corella D, Perez-Hoyos S, Saez M, Hervas A. 1997. Mortality as a function of temperature. A study in Valencia, Spain, 1991–1993. Int J Epidemiol 26:551–561.

Bates DV. 1992. Health indices of the adverse effects of air pollution: The question of coherence. Environ Res 59:336–349.

Bates DV, Baker-Anderson M, Sizto R. 1990. Asthma attack periodicity: A study of hospital emergency visits in Vancouver. Environ Res 51:51–70.

Bonvalot Y, Brook J. 1998. Station d'échantillonnage de l'air ambiant et zone d'influence: Protocole et rapport d'étude. Rapport de la direction de la santé publique de Montréal-centre, Unité de santé au travail/santé environnementale, 77 pages + annexes.

Borja-Aburto VH, Loomis DP, Bangdiwala SI, Shy CM, Rascon-Pacheco RA. 1997. Ozone, suspended particulates, and daily mortality in Mexico City. Am J Epidemiol 145:258–268.

Bourdages J. 1987. Description du système MedEcho 1982–1987. Minister of Health and Social Affairs, Quebec, Canada.

Boyd JT. 1960. Climate, air pollution, and mortality. Br J Prev Soc Med 14:123–135.

Braun-Fahrlander C, Ackermann-Leibrich U, Schwartz J, Gnehm HP, Rutishauser M, Wanner HU. 1992. Air pollution and respiratory symptoms in preschool children. Am Rev Respir Dis 145:42–47.

Breslow NE, Day NE. 1980. Statistical Methods in Cancer Research, Vol I, The Analysis of Case-Control Studies. International Agency for Research on Cancer, Lyon, France.

Brook JR, Dann TF, Burnett RT. 1997a. The relationship among TSP, PM_{10}, $PM_{2.5}$, and inorganic constituents of atmospheric particulate matter at multiple Canadian locations. J Air Waste Manage Assoc 46:2–19.

Brook JR, Wiebe AW, Woodhouse SW, Audette CV, Dann TF, Callaghan S, Piechowski M, Dabek-Zlotorzynska E, Dloughy JF. 1997b. Fine particle strong acidity, sulphate, PM_{10}, $PM_{2.5}$ and related gaseous species observed at multiple locations in Canada: Concentrations and spatial-temporal relationships. Atmos Environ 31:4223–4236.

Burnett RT, Brook JR, Cakmak S, Philips O, Raizenne ME, Stieb D, Vincent R, Ozkaynak H, Krewski D. 1998. The association between ambient CO levels and daily mortality in Toronto, Canada. J Air Waste Manage Assoc 48:689–700.

Burnett RT, Dales RE, Krewski D, Vincent R, Dann T, Brook JR. 1995. Associations between ambient particulate sulfate and admissions to Ontario hospitals for cardiac and respiratory diseases. Am J Epidemiol 142:15–22.

Burnett RT, Dales RE, Raizenne ME, Krewski D, Summers PW, Roberts GR, Raad-Young M, Dann T, Brook J. 1994.

Effects of low ambient levels of ozone and sulfate on frequency of respiratory admissions to Ontario hospitals. Environ Res 65:172–194.

Chestnut LG, Schwartz J, Savitz DA, Burchfiel CM. 1991. Pulmonary function and ambient particulate matter: Epidemiological evidence from NHANES I. Arch Environ Health 46:135–144.

Ciocco A, Thompson DJ. 1961. A follow-up on Donora ten years after: Methodology and findings. Am J Public Health 51:155–164.

Cohen AC Jr. 1961. Tables for maximum likelihood estimates: Singly truncated and singly censored samples. Technometrics 3:535–541.

Curb JD, Ford CE, Pressel S, Palmer M, Babcock C, Hawkins M. 1985. Ascertainment of vital status through the National Death Index and the Social Security Administration. Am J Epidemiol 121:754–766.

Dab W, Medina S, Quenel P, Le Moullec Y, le Tertre A, Thelot B, Monteil C, Lameloise P, Pirard P, Momas I, Ferry R, Festy B. 1996. Short-term respiratory health effects of ambient air pollution: Results of the APHEA project in Paris. J Epidemiol Community Health (Suppl 1) 50:S42–46.

de Faire U, Friberg L, Lorich U, Lundman T. 1976. A validation of cause-of-death certification in 1,156 deaths. Acta Med Scand 20:223–228.

Delfino RJ. Becklake MR. Hanley JA. 1993. Reliability of hospital data for population-based studies of air pollution. Arch Environ Health 48:140–146.

Delfino RJ, Becklake MR, Hanley JA, Singh B. 1994. Estimation of unmeasured particulate air pollution data for an epidemiological study of daily respiratory morbidity. Environ Res 67:20–38.

Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE. 1993. An association between air pollution and mortality in six US cities. N Engl J Med 329:1753–1759.

Dockery DW, Pope CA, III. 1994. Acute respiratory effects of particulate air pollution. Annu Rev Public Health 15:107–132.

Dockery DW, Schwartz J, Spengler JD. 1992. Air pollution and daily mortality: Associations with particulates and acid aerosols. Environ Res 59:362–373.

Dockery DW, Spengler JD. 1981a. Indoor-outdoor relationships of respirable sulfates and particles. Atmos Environ 15:335–343.

Dockery DW, Spengler JD. 1981b. Personal exposure to respirable particulates and sulfates. J Air Pollut Control Assoc 31:153–159.

Dockery DW, Ware JH, Ferris BG Jr, Speizer FE, Cook NR, Herman SM. 1982. Change in pulmonary function in children associated with air pollution episodes. J Air Pollut Control Assoc 32: 937–942.

Engel LW, Strauchen JA, Chiazze L Jr, Heid M. 1980. Accuracy of death certification in an autopsied population with specific attention to malignant neoplasms and vascular diseases. Am J Epidemiol 111:99–112.

Fairley D. 1990. The relationship of daily mortality to suspended particulates in Santa Clara County, 1980 to 1986. Environ Health Perspect 89:159–168.

Firket M. 1936. Fog along the Meuse Valley. Trans Faraday Soc 32:1192–1197.

Fleiss JL. 1981. Statistical Methods for Rates and Proportions. Wiley & Sons, New York NY.

Frank R, Tankersley C. 1997. The association between airborne particles and daily mortality rate: An explanatory hypothesis. Presented at the International Symposium on Health Effects of Particulate Matter in Ambient Air, April 23–25, 1997. Prague, Czech Republic.

Goldberg MS. 1996. Particulate air pollution and daily mortality: Who is at risk? J Aerosol Med 9:43–53.

Goldberg MS, Carpenter M, Thériault G, Fair M. 1993. The accuracy of ascertaining vital status in a historical cohort study of synthetic textiles workers using computerized record linkage to the Canadian Mortality Data Base. Can J Public Health 84:201–204.

Hald A. 1952. Statistical theory with engineering applications. Wiley & Sons, New York NY.

Hastie T, Tibshirani R, eds. 1990. Generalized Additive Models. Chapman & Hall, New York NY.

Health Effects Institute. 2000. Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality: A Special Report of the Institute's Particle Epidemiology Reanalysis Project. Health Effects Institute, Cambridge MA.

Heart and Stroke Foundation of Canada. 1999. The Changing Face of Heart Disease and Stroke in Canada. Heart and Stroke Foundation of Canada, Ottawa, Canada.

Hoek G, Brunekreef B. 1993. Acute effects of a winter air pollution episode on pulmonary function and respiratory symptoms of children. Arch Environ Health 4:328–335.

Hoek G, Brunekreef B. 1994. Effects of low-level winter air pollution concentrations on respiratory health of Dutch children. Environ Res 64:136–150.

Hornung RW, Reed LD. 1990. Estimation of average concentration in the presence of non-detectable values. Appl Occup Environ Hyg 5:46–51.

Ito K, Thurston GD. 1996. Daily PM_{10}/mortality associations: An investigation of at-risk subpopulations. J Expos Anal Environ Epidemiol 6:79–95.

Ito K, Thurston GD, Hayes C, Lippmann M. 1993. Associations of London, England, daily mortality with particulate matter, sulfur dioxide, and acidic aerosol pollution. Arch Environ Health 48:213–220.

Janssen NA, Hoek G, Brunekreef B, Harssema H, Mensink I, Zuidhof A. 1998. Personal sampling of particles in adults: Relation among personal, indoor, and outdoor air concentrations. Am J Epidemiol 147:537–547.

Katsouyanni K, Pantazopoulou A, Touloumi G, Tselepidaki I, Moustris K, Asimakopoulos D, Poulopoulou G, Trichopoulos D. 1993. Evidence for interaction between air pollution and high temperature in the causation of excess mortality. Arch Environ Health 48:235–242.

Kinney PL, Ito K, Thurston GD. 1995. A sensitivity analysis of mortality/PM_{10} associations in Los Angeles. Inhalation Toxicol 7:59–69.

Kinney PL, Ozkaynak H. 1991. Associations of daily mortality and air pollution in Los Angeles County. Environ Res 54:99–120.

Koenig JQ, Larson TV, Hanley QS, Rebolledo V, Dumler K., Checkoway H, Wang SZ, Lin D, Pierson WE. 1993. Pulmonary function changes in children associated with fine particulate matter. Environ Res 63: 26–38l.

Koutrakis P, Wolfson JM, Slater JL, Brauer M, Spengler JD, Stevens RK. 1988. Evaluation of an annual denuder/filterpack system to collect acidic aerosols and gases. Environ Sci Technol 22:1463–1468.

Leech JA, Wilby K, McMullen E, Laporte K. 1996. The Canadian human activity pattern survey: Report of methods and population surveyed. Chronic Dis Can 17:118–123.

Lipfert FW, Hammerstrom T. 1992. Temporal patterns in air pollution and hospital admissions. Environ Res 59:374–399.

Logan WPD. 1953. Mortality in the London fog incident. Lancet i:336–338.

Marshall JR. 1990. Data dredging and noteworthiness. Epidemiology 1:5–7.

Mayo N, Danys I, Carlton J. 1993. Accuracy of hospital discharge coding for stroke. Can J Cardiol (Suppl D) 9:121–124.

Mazumdar S, Sussman N. 1983. Relationships of air pollution to health: Results from the Pittsburgh study. Arch Environ Health 38:17–24.

Michelozzi P, Forastiere F, Fusco D, Perucci CA, Ostro B, Ancona C, Pallotti G. 1998. Air pollution and daily mortality in Rome, Italy. Occup Environ Med 55:605–610.

Moolgavkar SH, Luebeck EG, Hall TA, Anderson EL. 1995. Particulate air pollution, sulfur-dioxide, and daily mortality: A reanalysis of the Steubenville data. Inhalation Toxicol 7:35–44.

Muir D, Laxen DPH. 1995. Black smoke as a surrogate for PM_{10} in health studies. Atmos Environ 29:959–962.

Newcombe HB, Smith ME, Howe GR, Mingay J, Strugnell A, Abbatt JD. 1983. Reliability of computerized versus manual death searches in a study of the health of Eldorado uranium workers. Comput Biol Med 13:157–69.

Ostro BD. 1983. The effects of air pollution on work loss and morbidity. J Environ Econ Manag 10:371–382.

Ostro BD. 1987. Air pollution and morbidity revisited: A specification test. J Environ Econ Manage 14:87–98.

Ostro BD. 1990. Association between morbidity and alternative measures of particulate matter. Risk Anal 10:421–427.

Ostro BD, Lipsett MJ, Wiener MB, Selner JC. 1991. Asthmatic response to airborne acid aerosols. Am J Public Health 1:694–702.

Ostro BD, Rothschild S. 1989. Air pollution and acute respiratory morbidity: An observational study of multiple pollutants. Environ Res 50: 238–247.

Ostro B, Sanchez JM, Aranda C, Eskeland GS. 1996. Air pollution and mortality: Results from a study of Santiago, Chile. J Expos Anal Environ Epidemiol 6:97–114.

Özkaynak H, Schatz AD, Thurston GD, Isaacs RG, Husar RB. 1985. Relationships between aerosol extinction coefficients derived from airport visual range observations and alternative measures of airborne particulate matter. J Air Pollut Control Assoc 35:1176–1185.

Paino JH. 1993. Carbon monoxide saturation study in Boston (February 19–March 19, 1993). Quality Assurance Section, Air Quality Surveillance Branch.

Percy C, Stanek E III, Gloeckler L. 1981. Accuracy of cancer death certificates and its effect on cancer mortality statistics. Am J Public Health 71:242–250.

Pleasant M. 1994. Philadelphia diesel particulate monitoring study. ManTech environmental technology report. US Environmental Protection Agency Contract Number 68-D0-0106.

Pope CA III. 1989a. Respiratory hospital admissions associated with PM_{10} pollution in Utah, Salt Lake, and Cache Valleys. Arch Environ Health 46:90–97.

Pope CA III. 1989b. Respiratory disease associated with community air pollution and a steel mill, Utah Valley. Am. J Public Health 79:623–628.

Pope CA III, Dockery DW. 1992. Acute health effects of PM_{10} pollution on symptomatic and asymptomatic children. Am Rev Respir Dis 145:1123–1128.

Pope CA III, Dockery DW, Spengler JD, Raizenne ME. 1991. Respiratory health and PM_{10} pollution: A daily time-series analysis. Am Rev Respir Dis 144:68–674.

Pope CA III, Kanner RE. 1993. Acute effects of PM_{10} pollution on pulmonary function of smokers with mild to moderate chronic obstructive pulmonary disease. Am Rev Respir Dis 147:1336–1340.

Pope CA III, Schwartz J, Ransom MR. 1992. Daily mortality and PM_{10} pollution in Utah Valley. Arch Environ Health 47:211–217.

Pope CA III, Thun MJ, Namboodiri MM, Dockery DW, Evans JS, Speizer FE, Heath CW Jr. 1995. Particulate air pollution as a predictor of mortality in a prospective study of US adults. Am J Respir Crit Care Med 151:669–674.

Priestly MB. 1981. Spectral Analysis of Time Series. Academic Press, Orlando FL.

Rahlenbeck SI, Kahl H. 1996. Air population and mortality in East Berlin during the winters of 1981 to 1989. Int J Epidemiol 25:1220–1226.

Ransom MR, Pope CA III. 1992. Elementary school absences and PM_{10} pollution in Utah Valley. Environ Res 58:204–219.

Roemer W, Hoek G, Brunekreef B. 1993. Effect of ambient winter in air pollution on respiratory health of children with chronic respiratory symptoms. Am Rev Respir Dis 147:118–124.

Rothman KJ. 1990. No adjustments are needed for multiple comparisons. Epidemiology 1:43–47.

Saldiva PHN, Pope CA III, Schwartz J, Dockery DW, Lichtenfels AJ, Salge JM, Barone I, Bohm GM. 1995. Air pollution and mortality in elderly people: A time-series study in Sao Paulo, Brazil. Arch Environ Health 50:159–163.

Samet J, Zeger S, Kelsall J, Xu J, Kalkstein L. 1998. Does weather confound or modify the association of particulate air pollution with mortality? An analysis of the Philadelphia data, 1973 to 1980. Environ Res 77:9–19.

Samet JM, Zeger SL, Berhane K. 1995. The association of mortality and particulate air pollution. In: Particulate Air Pollution and Daily Mortality, Replication and Validation of Selected Studies, The Phase I Report of the Particle Epidemiology Evaluation Project. Health Effects Institute, Cambridge MA.

Samet JM, Speizer FE, Bishop Y, Spengler JD, Ferris BG Jr. 1981. The relationship between air pollution and emergency room visits in an industrial community. J Air Pollut Control Assoc 31:236–240.

Schimmel H, Murawski TJ. 1976. The relation of air pollution to mortality. J Occup Med 18:316–333.

Schnatter AR, Acquavella JF, Thomson FS, Donaleski D. 1990. An analysis of death ascertainment and follow-up through Statistics Canada's Mortality Data Base system. Can J Public Health 81:60–65.

Schwartz J. 1991. Particulate air pollution and daily mortality: A synthesis. Public Health Rev 19:39–60.

Schwartz J. 1993. Air pollution and daily mortality in Birmingham, Alabama. Am J Epidemiol 137:1136–1147.

Schwartz J. 1994a. Air pollution and daily mortality: A review and meta analysis. Environ Res 64:36–52.

Schwartz J. 1994b. Total suspended particulate matter and daily mortality in Cincinnati, Ohio. Environ Health Perspect 102:186–189.

Schwartz J. 1994c. Air pollution and hospital admissions for the elderly in Detroit. Am J Respir Crit Care Med 150:648–655.

Schwartz J. 1994d. Air pollution and hospital admissions for the elderly in Birmingham, Alabama. Am J Epidemiol 139:589–590.

Schwartz J, Dockery DW. 1992. Particulate air pollution and daily mortality in Steubenville, Ohio. Am J Epidemiol 135:12–19.

Schwartz J, Dockery DW, Neas LM. 1996. Is daily mortality associated specifically with fine particles? J Air Waste Manage Assoc 46:927–939.

Schwartz J, Marcus A. 1990. Mortality and air pollution in London: A time-series analysis. Am J Epidemiol 131:185–194.

Seaton A, MacNee W, Donaldson K, Godden D. 1995. Particulate air pollution and acute health effects. Lancet 345:176–178.

Shannon H, Jamieson E, Walsh C, Julian J, Fair M, Buffet A. 1989. Comparison of individual follow-up and computerized record linkage using the Canadian Mortality Data Base. Can J Public Health 80:54–57.

Shrenk HH, Heimann H, Clayton GD, et al. 1949. Air Pollution in Donora, PA: Epidemiology of the Unusual Smog Episode of October 1948: Preliminary Report. Public Health Bulletin Number 306. US Public Health Service, Washington DC.

Spengler JD, Dockery DW, Turner W, Wolfson M, Ferris BG Jr. 1981. Long-term measurements of respirable sulfates and particles inside and outside homes. Atmos Environ 15:23–30.

Spengler JD, Sexton K. 1983. Indoor air pollution: A public health perspective. Science 221:9–17.

Spix C, Heinrich J, Dockery D, Schwartz J, Volksch G, Schwinkowski K, Collen C, Wichmann HE. 1993. Air pollution and daily mortality in Erfurt, East Germany, 1980–1989. Environ Health Perspect 101:518–526.

Spix C, Wichmann HE. 1996. Daily mortality and air pollutants: Findings from Koln, Germany. J Epidemiol Community Health (Suppl 1) 50:S52–58.

Stampfer MJ, Willett WC, Speizer FE, Dysert DC, Lipnick R, Rosner B, Hennekens CH. 1984. Test of the national death index. Am J Epidemiol 119:837–839.

Styer P, McMillan N, Gao F, Davis J, Sacks J. 1995. The effect of airborne particulate matter on daily death counts. Environ Health Perspect 103:490–497.

Sunyer J, Castellsague J, Saez M, Tobias A, Anto JM. 1996. Air pollution and mortality in Barcelona. J Epidemiol Community Health (Suppl 1) 50:S76–80.

Sunyer J, Saez M, Murillo C, Castellsague J, Martinez F, Anto JM. 1993. Air pollution and emergency room admissions for chronic obstructive pulmonary disease: A 5-year study. Am J Epidemiol 137:701–705.

Thomas DC, Siemiatycki J, Dewar R, Robins J, Goldberg M, Armstrong BG. 1985. The problem of multiple inference in studies designed to generate hypotheses. Am J Epidemiol 122:1080–1095.

Thurston GD, Ito K., Lippmann M. 1993. The role of particulate mass vs. acidity in the sulfate-respiratory hospital admissions association: Preprint 93-11.03. 86th Annual Meeting of the Air & Waste Management Association, June 13–18, 1993. Denver CO.

Thurston GD, Ito K, Kinney PL, Lippmann M. 1992. A multi-year study of air pollution and respiratory hospital admissions in three New York state metropolitan areas: Results for 1988 and 1989 summers. J Expos Anal Environ Epidemiol 2:429–450.

Touloumi G, Samoli E, Katsouyanni K. 1996. Daily mortality and "winter type" air pollution in Athens, Greece: A time-series analysis within the APHEA project. J Epidemiol Community Health (Suppl 1) 50:S47–51.

US Environmental Protection Agency. 1996. National Air Quality and Emissions Trends Report, 1995. Office of Air Quality Planning and Standards, Research Triangle Park NC.

Verhoeff AP, Hoek G, Schwartz J, van Wijnen JH. 1996. Air pollution and daily mortality in Amsterdam. Epidemiology 7:225–230.

Vigotti MA, Rossi G, Bisanti L, Zanobetti A, Schwartz J. 1996. Short-term effects of urban air pollution on respiratory health in Milan, Italy, 1980 to 1989. J Epidemiol Community Health (Suppl 1) 50:S71–75.

Wallace L. 1996. Indoor particles: A review. J Air Waste Manage Assoc 46:98–126.

Wentworth DN, Neaton JD, Rasmussen WL. 1983. An evaluation of the Social Security Administration Master Beneficiary Record File and the National Death Index in the ascertainment of vital status. Am J Public Health 73:127–1274.

Whittemore AS, Korn EL. 1980. Asthma and air pollution in the Los Angeles Area. Am J Public Health 70:687–696.

Wojtyniak B, Piekarski T. 1996. Short-term effects of air pollution on mortality in Polish urban populations: What is different? J Epidemiol Community Health (Suppl 1) 50:S36–41.

Zeger SL, Thomas D, Dominici F, Samet JM, Schwartz J, Dockery D, Cohen A. 2000. Exposure measurement error in time-series studies of air pollution: Concepts and consequences. Environ Health Perspect 108:419–426.

Zidek JV, Wong H, Le HD, Burnett R. 1996. Causality, measurement error and multicollinearity in epidemiology. Environmetrics 7:441–451.

Zmirou D, Barumandzadeh T, Balducci F, Ritter P, Laham G, Ghilardi JP. 1996. Short-term effects of air pollution on mortality in the city of Lyon, France, 1985 to 1990. J Epidemiol Community Health (Suppl 1) 50:S30–35.

APPENDIX A. Distributions of Variables for the Study Population

Table A.1 shows selected characteristics of deceased study subjects. For those subjects who were linked to the QHIP, Table A.1 shows that the annual number of deaths increased over this period, with an average annual increase of about 142 deaths (average of 1.01% per annum). This increase in the number of deaths occurred probably because of the increasing age of Montrealers rather than from changes in personal risk factors. The distribution of causes of death is in accord with expectation. Table A.2 shows that a larger proportion of deaths in men were from accidents and cancer and a greater proportion of deaths in women were from cardiovascular diseases. Table A.3 shows the distribution of underlying causes of death by subjects' ages.

Table A.1. Distribution of Selected Variables for 140,939 Deceased Subjects

Characteristic	Deaths	Percentage
Year of Death		
1984	13,289	9.4
1985	13,684	9.7
1986	13,761	9.8
1987	14,154	10.0
1988	13,928	9.9
1989	14,371	10.2
1990	13,933	9.9
1991	14,490	10.3
1992	14,248	10.1
1993	15,081	10.7
Sex		
Men	72,752	51.6
Women	68,187	48.4

(Table continues next column)

Table A.1 *(continued).* Distribution of Selected Variables for 140,939 Deceased Subjects

Characteristic	Deaths	Percentage
Age		
≤ 1	275	0.2
2–9	296	0.2
10–19	570	0.4
20–34	3,586	2.5
35–64	31,632	22.4
65–74	34,531	24.5
≥ 75	70,049	49.7
Marital Status		
Single	25,881	18.4
Married	59,958	42.5
Widowed	45,869	32.5
Divorced	6,299	4.5
Separated	2,932	2.1
Underlying Cause of Death[a]		
Neoplasms	42,140	29.9
Digestive	11,340	8.0
Lung	11,322	8.0
Female breast	3,807	2.7
Others	15,671	11.1
Cardiovascular diseases	57,296	40.7
Acute coronary artery disease	21,578	15.3
Chronic coronary artery disease	12,735	9.0
Coronary disease	34,313	24.3
Cerebrovascular disease	9,480	6.7
Others	13,503	9.6
Respiratory diseases	11,394	8.1
Digestive diseases	5,802	4.1
Other Causes	17,272	12.3
AIDS	1,472	1.0
Diabetes	3,677	2.6
Renal diseases	1,798	1.3
Neurological conditions	4,256	3.0
All Nonaccidental Causes	133,904	95.0
Accidents	7,035	5.0
All Causes	140,939	100.0

[a] Definitions from ICD-9: neoplasms, ICD-9 140–239; circulatory diseases, 390–459; respiratory, 460–519, digestive, 520–579. Other causes are represented by all remaining rubrics and include AIDS, 042; diabetes, 250; renal and kidney disease, 580–593; neurological conditions, 013, 036, 046, 269, 290, 294, 310, 320–337, 342, 348–349, 352, 742; digestive cancer, 151–159; lung cancer, 162; breast cancer, 174; acute coronary artery disease, 410–411; chronic coronary artery disease, 412–414; coronary disease, 410–414; and cerebrovascular disease, 430–438. This table includes data on subjects eligible for study, which is a subset of Table 4 (147,278 subjects).

Table A.2. Distribution of Underlying Causes of Death by Sex for 140,939 Deceased Residents of Montreal Included in This Report, 1984 to 1993[a]

	Women		Men	
Cause of Death	Deaths	Percentage	Deaths	Percentage
Cardiovascular	29,493	43.3	27,803	38.2
Acute coronary artery disease	9,955	14.6	11,623	16.0
Chronic coronary artery disease	6,421	9.4	6,314	8.7
Coronary disease	16,376	24.0	17,937	24.7
Cerebrovascular disease	5,650	8.3	3,830	5.3
Others	7,467	11.0	6,036	8.3
Neoplasms	19,673	28.9	22,467	30.9
Digestive	5,567	8.2	5,773	7.9
Lung	3,420	5.0	7,902	10.9
Female breast	3,807	5.6	0	0.0
Others	6,879	10.1	8,792	12.1
Respiratory	5,036	7.4	6,358	8.7
Nonmalignant Digestive	2,648	3.9	3,154	4.3
Other Causes	8,779	12.9	8,493	11.7
AIDS	117	0.2	1,355	1.9
Diabetes	1,981	2.9	1,696	2.3
Renal diseases	960	1.4	838	1.2
Neurological conditions	2,508	3.7	1,748	2.4
All Nonaccidental Causes	65,629	96.2	68,275	93.8
All Causes	68,187	100.0	72,752	100.0

[a] Definitions from ICD-9: neoplasms, 140–239; circulatory diseases, 390–459; respiratory, 460–519; and digestive, 520–579. Other causes are represented by all remaining rubrics and include AIDS, 042; diabetes, 250; renal and kidney disease, 580–593; neurological conditions, 013, 036, 046, 269, 290, 294, 310, 320–337, 342, 348–349, 352, 742; digestive cancer, 151–159; lung cancer, 162; breast cancer, 174; acute coronary artery disease, 410–411; chronic coronary artery disease, 412–414; coronary disease, 410–414; and cerebrovascular disease, 430–438.

Table A.3. Distribution of Underlying Causes of Death by Age for 140,939 Deceased Residents of Montreal Included in This Report, 1984 to 1993[a]

	0–9 Years		10–19 Years		20–64 Years		≥ 65 Years	
Cause of Death	Deaths	Percent	Deaths	Percent	Deaths	Percent	Deaths	Percent
Cardiovascular	32	5.6	29	5.1	9,583	27.2	47,652	45.6
Acute coronary artery disease	1	0.2	3	0.5	4,719	13.4	16,855	16.1
Chronic coronary artery disease	0	0.0	2	0.4	1,689	4.8	11,044	10.6
Coronary disease	1	0.2	5	0.9	6,408	18.2	27,899	26.7
Cerebrovascular disease	6	1.1	7	1.2	1,277	3.6	8,190	7.8
Others	25	4.4	17	3.0	1,898	5.4	11,563	11.1
Neoplasms	89	15.6	89	15.6	13,845	39.3	28,117	26.9
Digestive	1	0.2	1	0.2	3,014	8.6	8,324	8.0
Lung cancer	0	0.0	1	0.2	4,260	12.1	7,061	6.8
Female breast	0	0.0	0	0.0	1,637	4.6	2,170	2.1
Others	88	15.4	87	15.3	4,934	14.0	10,562	10.1
Respiratory	24	4.2	16	2.8	1,388	3.9	9,966	9.5
Nonmalignant Digestive	14	2.5	4	0.7	1,690	4.8	4,094	3.9
Other Causes	285	49.9	113	19.8	4,555	12.9	12,319	11.8
AIDS	9	1.6	3	0.5	1,441	4.1	19	0.0
Diabetes	0	0.0	0	0.0	730	2.1	2,947	2.8
Renal diseases	0	0.0	3	0.5	230	0.7	1,565	1.5
Neurologic conditions	49	8.6	33	5.8	390	1.1	3,784	3.6
All Nonaccidental Causes	444	77.8	251	44.0	31,061	88.2	102,148	97.7
All Causes	571	100.0	570	100.0	35,218	100.0	104,580	100.0

[a] Definitions from ICD-9: neoplasms, 140–239; circulatory diseases, 390–459; respiratory, 460–519; and digestive, 520–579. Other causes are represented by all remaining rubrics and include AIDS, 042; diabetes, 250; renal and kidney disease, 580–593; neurological conditions, 013, 036, 046, 269, 290, 294, 310, 320–337, 342, 348–349, 352, 742; digestive cancer, 151–159; lung cancer, 162; breast cancer, 174; acute coronary artery disease, 410–411; chronic coronary artery disease, 412–414; coronary disease, 410–414; and cerebrovascular disease, 430–438.

APPENDIX B. Time Series Plots for Pollutants, Weather Variables, and Mortality

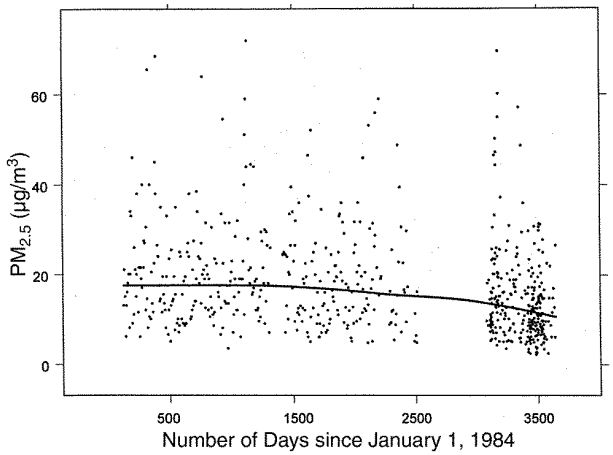

Figure B.1. Mean daily $PM_{2.5}$. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

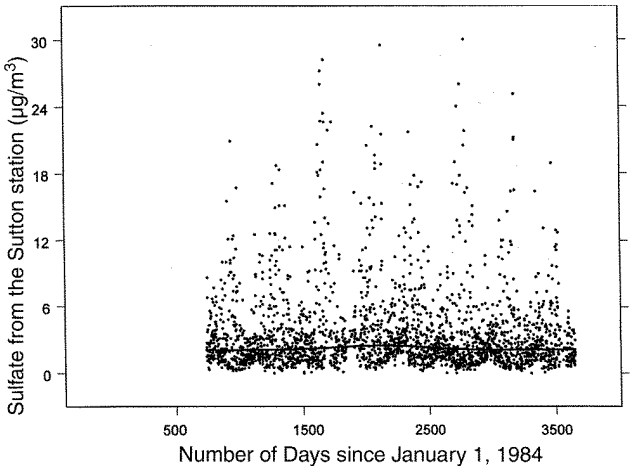

Figure B.2. Mean daily sulfate from the Sutton monitoring station. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

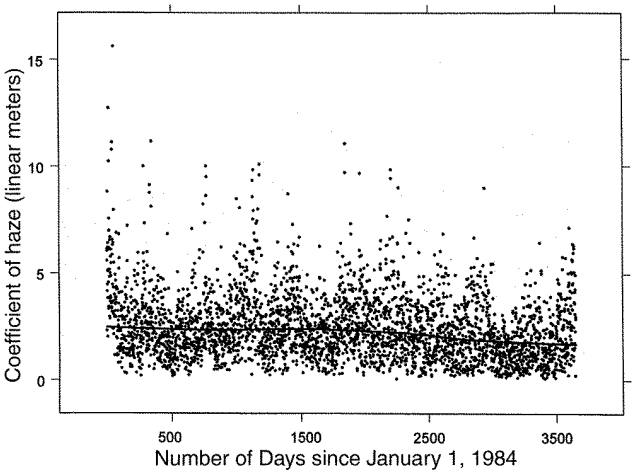

Figure B.3. Mean daily coefficient of haze. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

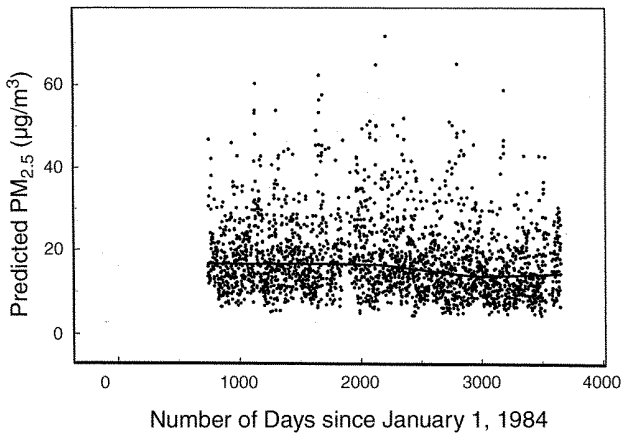

Figure B.4. Mean daily predicted PM2.5. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

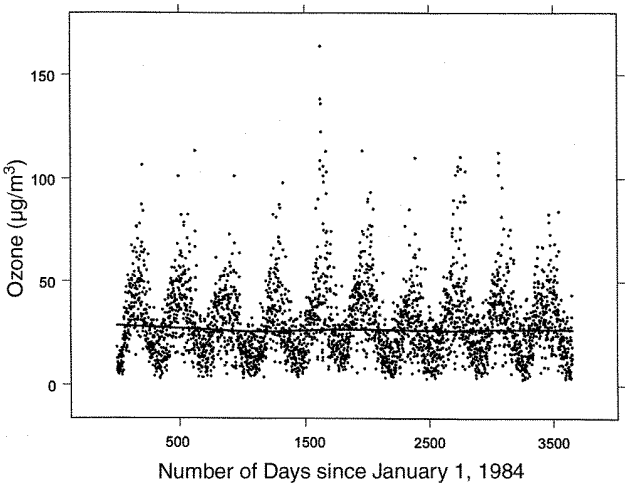

Figure B.5. Mean daily ozone. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

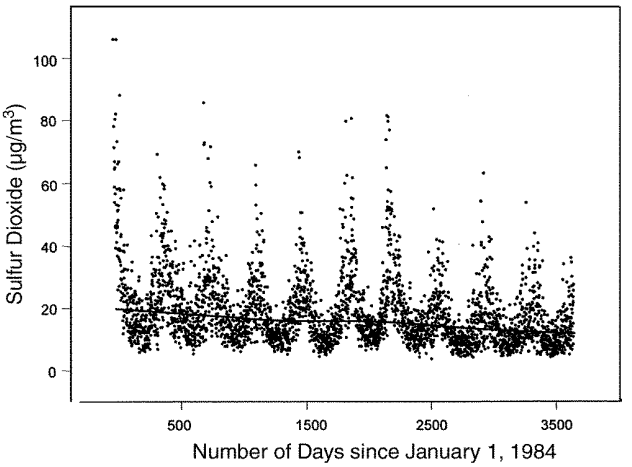

Figure B.6. Mean daily sulfur dioxide. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

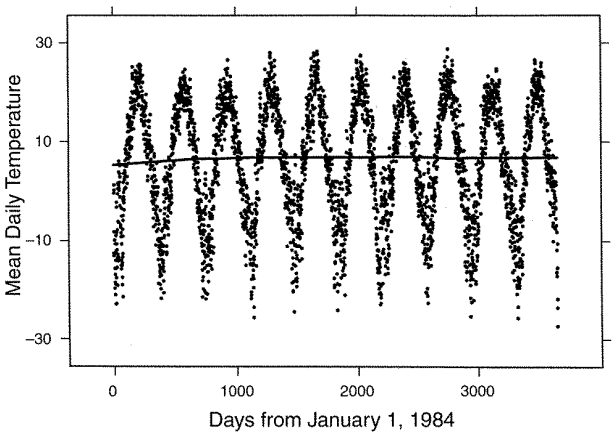

Figure B.7. Mean daily temperature. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

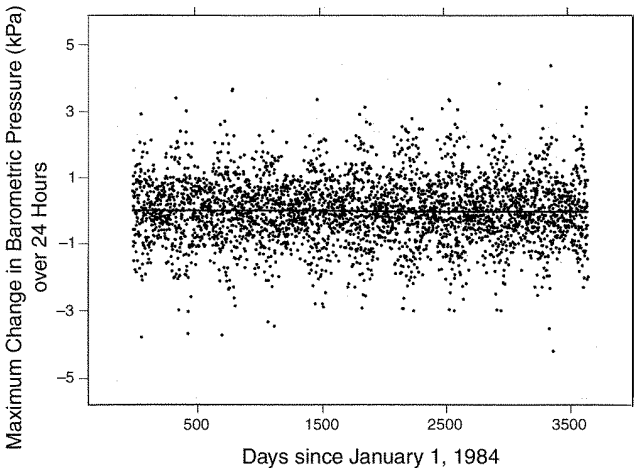

Figure B.10. Change in barometric pressure from the previous 24 hours. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

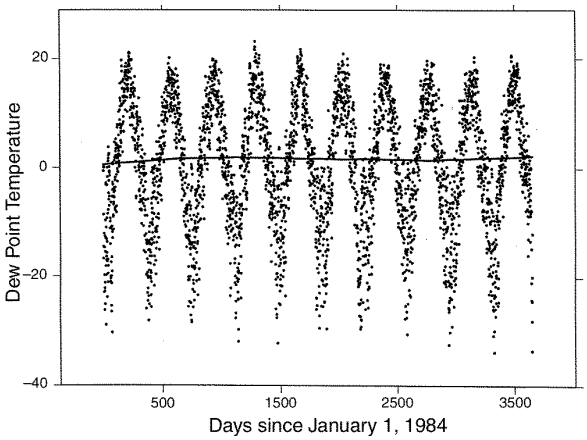

Figure B.8. Mean daily dew point temperature. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

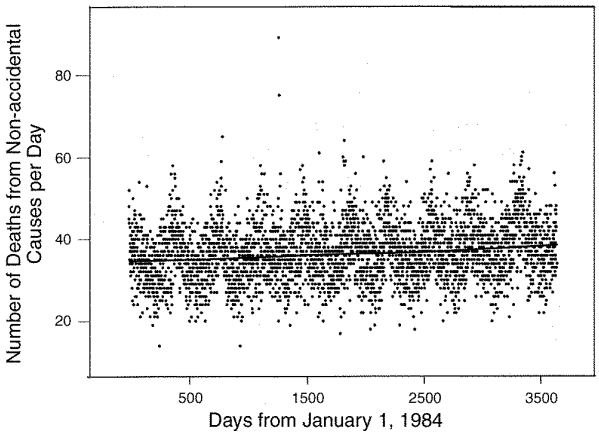

Figure B.11. Daily deaths from nonaccidental causes. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

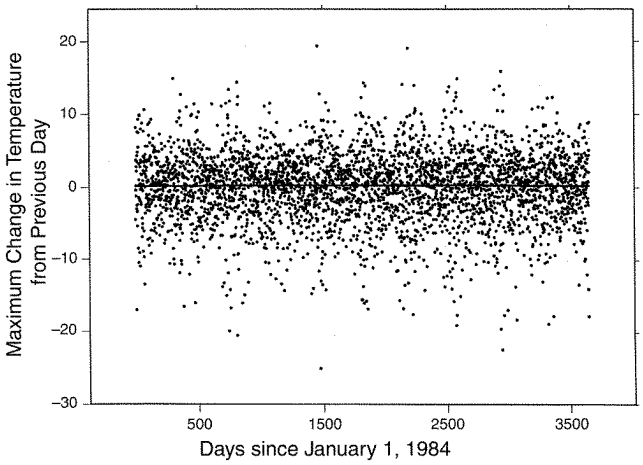

Figure B.9. Maximum change in temperature from the previous day. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

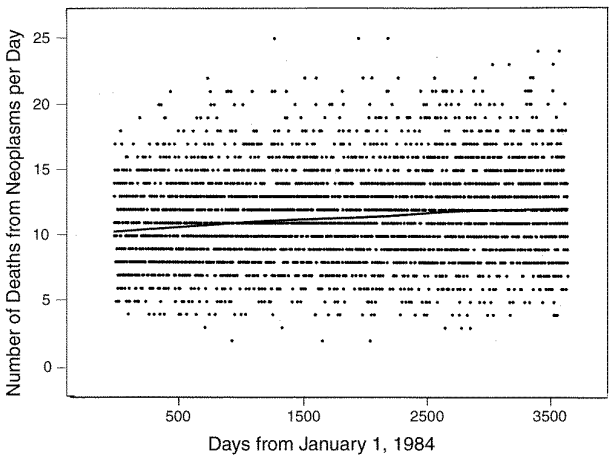

Figure B.12. Daily deaths from neoplasms. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

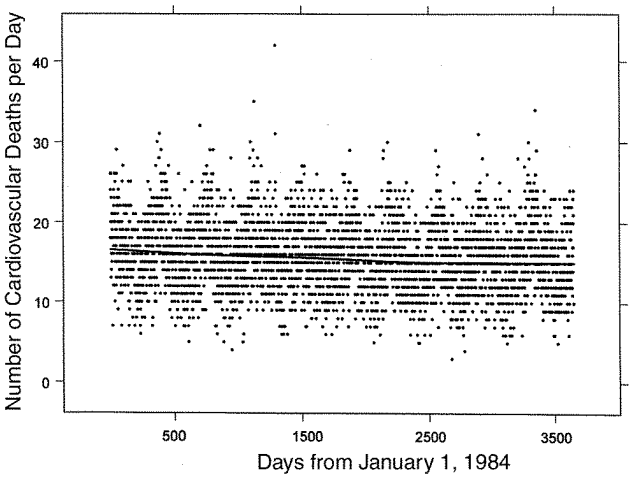

Figure B.13. Daily deaths from cardiovascular diseases. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

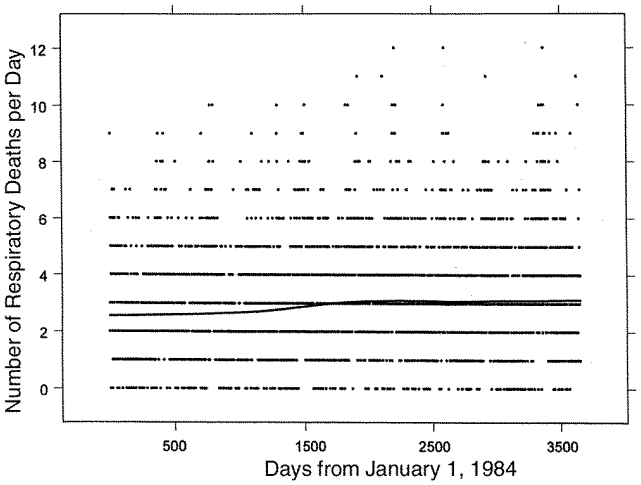

Figure B.14. Daily deaths from respiratory diseases. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

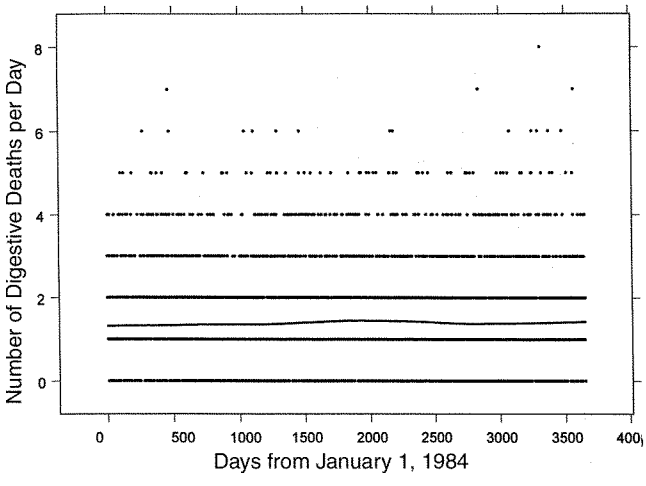

Figure B.15. Daily deaths from non-malignant digestive diseases. The solid line is the LOESS smooth representing the long-term trend in the data

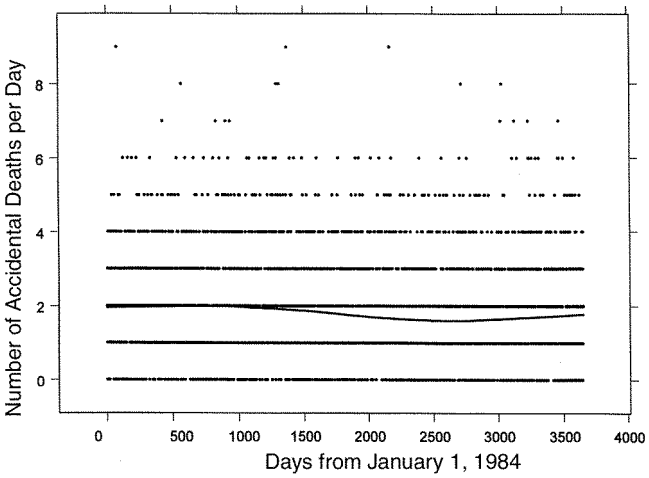

Figure B.16. Daily accidental deaths. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

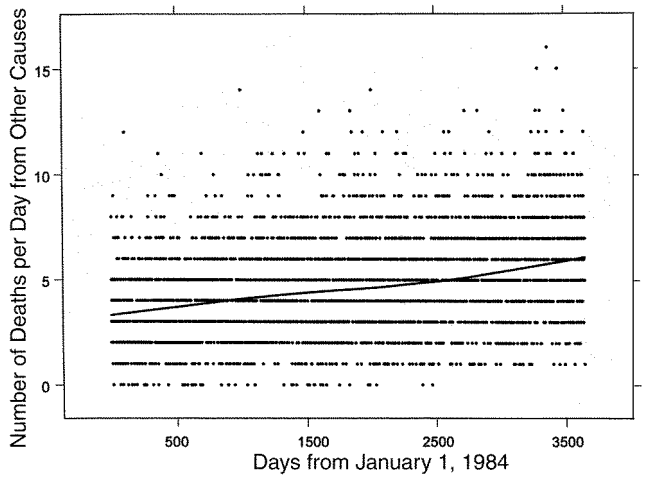

Figure B.17. Deaths from all other causes. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

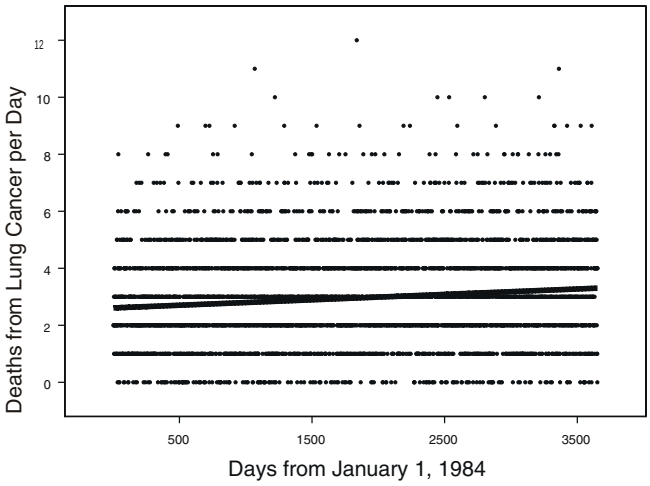

Figure B.18. Deaths from lung cancer. the solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

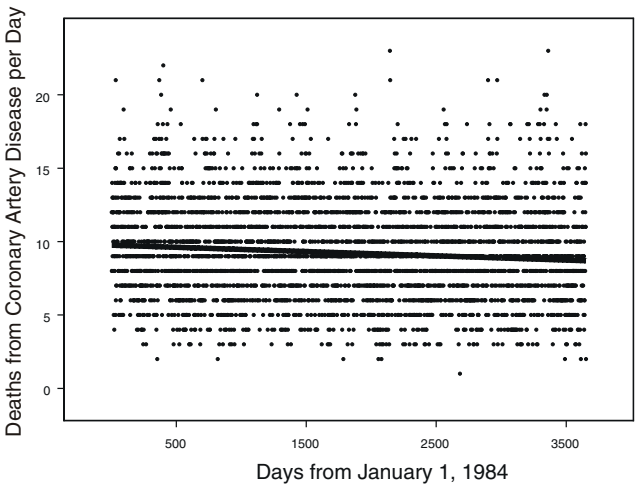

Figure 19. Deaths from coronary artery disease. The solid line is the LOESS smooth representing the long-term trend in the data (span of 67%).

APPENDIX C. Description of Environmental Pollutants and Weather Variables

Table C.1 describes the monitoring stations, and Tables C.2 through C.6 show the Pearson correlation coefficients.

An appropriate metric of TSP and PM would be the daily means across all monitoring stations. We attempted to confirm this empirically through a small pilot study to determine the extent of spatial variation of levels of TSP and PM_{10} around the fixed monitoring stations (Table C.7). This pilot study was conducted in Montreal in July and August of 1996 and funded by the Montreal Public Health Department (Bonvalot and Brook 1998).

We selected one station at the intersection of two major highways in the west end of the city (the Decarie Boulevard monitoring station) and the other station in a residential neighborhood in the east end of the city (Botanical Gardens monitoring station). We obtained 22-hour integrated samples of TSP and PM_{10} with portable MiniVol samplers (AirMetrics, Eugene OR) working at a constant flow rate of 5 L/min. These monitors were used previously by the EPA in saturation studies (Anonymous 1993; Paino 1993; Pleasant 1994; Adams et al 1995).

We used a systematic sampling design to assess the spatial representativeness of the fixed monitoring stations. Five portable monitors were located along concentric circles at 1 and 3 km radii from the two fixed monitoring stations. Upwind and downwind measurements of TSP and PM_{10} along one radius were taken simultaneously each day. Samples were taken for about three weeks around the Botanical Gardens monitoring station (residential district) and then for three weeks in the vicinity of the Decarie Boulevard monitoring station (at the junction of two expressways). Gravimetric measurements of the filters were made using standard techniques at Environment Canada laboratories.

Table C.7 shows that, in the residential area, we observed practically no difference in mean concentrations of TSP between the fixed monitoring site and measurements made at distances of 1 km and 3 km. However, for measurements made near the intersection of the two major highways (Decarie Boulevard station), we found a large difference between the fixed monitoring site and measurements made both at 1 km (mean of 76.1 $\mu g/m^3$ versus 51.5 $\mu g/m^3$, respectively) and 3 km distance (56.0 $\mu g/m^3$ versus 35.9 $\mu g/m^3$, respectively). On the other hand, for PM_{10}, we observed no important differences in measurements made at the central site and at 1 km or 3 km in either sampling area.

For TSP, we found that

- levels in residential areas can be represented by fixed monitoring stations located in other residential neighborhoods within 6 km,
- levels observed in areas with heavy traffic are significantly higher than those observed at 1 km or 3 km distance, and
- the extent of spatial variability is time-dependent.

These observations suggest that TSP levels are influenced heavily by traffic and that these levels are reduced dramatically away from major traffic arteries. For PM_{10}, the spatial distribution was much more homogeneous. The study also showed that for areas not near heavy traffic, the fixed monitoring station located downtown (Amherst and Ontario Streets) is representative of levels as far off as 14 km from the site (Brook et al 1997a).

We conclude that for PM_{10} and $PM_{2.5}$, and probably for sulfate, to use the mean value of the two monitoring stations is likely to be representative. Although we noted considerable spatial variation in levels of TSP, one must still account for a large segment of the population of Montreal who live within 2 km of highways, so we decided to use the average across all monitoring stations.

Table C.1. Description of Monitoring Stations in Montreal, Quebec, 1984 to 1993[a]

Pollutant	Monitoring Stations	Days with Measurements	Days with Missing Values	Average of Daily Means	Range of Pearson Correlation Coefficients Between Stations
COH	2	245	101	3.55	0.30–0.68
	3	2,145	711	1.72	0.46–0.64
	10	487	2,010	2.45	0.41–0.71
	12	2,273	979	2.17	0.43–0.72
	19	246	116	1.61	0.39–0.71
	23	937	897	1.21	0.30–0.60
	28	2,773	876	4.18	0.22–0.53
	29	2,929	718	1.86	0.22–0.68
	60	2,138	1,133	1.42	0.29–0.71
	61	3,366	287	3.64	0.46–0.64
	68	3,157	496	1.53	0.30–0.72
TSP	1	478	128	32.88	0.39–0.58
	3	517	91	53.11	0.50–0.71
	6	527	78	77.89	0.31–0.67
	12	539	70	53.74	0.41–0.81
	13	557	52	58.96	0.38–0.82
	15	478	129	41.89	0.36–0.90
	19	518	91	45.12	0.39–0.89
	23	525	83	50.78	0.29–0.77
	28	473	136	79.29	0.24–0.60
	29	506	102	47.51	0.31–0.64
	42	502	105	41.47	0.26–0.78
	44	556	53	88.33	0.40–0.76
	49	449	158	35.37	0.24–0.83
	50	520	88	45.83	0.39–0.90
	52	527	82	42.38	0.42–0.78
	58	542	67	62.55	0.48–0.84
	60	470	139	41.82	0.33–0.82
	68	503	105	53.69	0.45–0.82
	86	326	67	56.02	0.31–0.79
Sulfate from TSP	1	380	167	2.28	0.26–0.53
	3	508	100	4.57	0.49–0.63
	6	440	165	5.97	0.47–0.86
	11	112	9	3.58	0.26–0.89
	12	528	81	5.04	0.51–0.84
	13	545	64	4.89	0.49–0.90
	28	456	153	3.79	0.51–0.75
	29	471	137	2.53	0.41–0.81
	44	55	4	4.56	0.49–0.96
	50	455	93	5.06	0.51–0.84
	58	57	2	4.34	0.48–0.96
	60	458	151	4.22	0.50–0.91
	68	493	115	4.88	0.49–0.89

(Table continues next page)

[a] PM measured by Environment Canada as part of the National Air Pollution Surveillance Program. All other pollutants measured by the Montreal Urban Community.

[b] Not in Montreal; measured 1986 to 1993.

Table C.1 *(continued).* Description of Monitoring Stations in Montreal, Quebec, 1984 to 1993[a]

Pollutant	Monitoring Stations	Days with Measurements	Days with Missing Values	Average of Daily Means	Range of Pearson Correlation Coefficients Between Stations
PM_{10}	Ontario St	577	256	27.80	0.65
	Duncan St	315	252	44.54	0.65
Sulfate from PM_{10}	Ontario St	397	191	4.59	0.92
	Duncan St	321	246	4.56	0.92
$PM_{2.5}$	Ontario St	611	222	16.22	0.86
	Duncan St	321	246	21.05	0.86
Sulfate from $PM_{2.5}$	Ontario St	423	165	4.24	0.92
	Duncan St	321	246	3.99	0.92
Sulfate measured at Sutton station[b]	Sutton	2,680	236	3.35	0.27–0.87
SO_2	1	3,195	458	19.16	0.20–0.72
	2	2,609	676	19.44	0.28–0.75
	3	3,420	233	30.70	0.10–0.29
	10	2,135	1,143	17.12	0.10–0.63
	12	3,134	514	16.99	0.26–0.73
	19	2,144	625	16.40	0.08–0.68
	21	1,696	799	15.08	0.29–0.75
	23	1,759	652	11.10	0.08–0.34
	28	2,701	935	20.45	0.12–0.59
	29	2,825	822	15.14	0.20–0.62
	60	2,660	948	12.39	0.18–0.60
	61	3,513	135	20.50	0.24–0.70
	68	3,443	210	13.56	0.16–0.51
O_3	1	3,086	563	28.77	0.67–0.81
	3	2,978	675	31.16	0.53–0.74
	12	3,340	308	27.14	0.69–0.86
	28	2,437	1,215	18.03	0.53–0.75
	29	3,220	427	30.01	0.65–0.84
	49	3,031	558	43.12	0.53–0.80
	60	2,872	610	37.56	0.59–0.80
	61	3,070	583	16.62	0.53–0.76
	68	3,343	230	29.07	0.68–0.86
NO	1	2,956	697	27.18	0.62–0.72
	3	2,966	687	20.20	0.46–0.71
	12	2,999	642	32.67	0.56–0.72
	28	2,637	978	89.88	0.28–0.67
	29	2,719	928	40.84	0.28–0.81
	60	2,113	830	21.37	0.44–0.81
	61	3,484	169	75.70	0.43–0.68
	68	2,972	681	21.22	0.47–0.66

(Table continues next page)

[a] PM measured by Environment Canada as part of the National Air Pollution Surveillance Program. All other pollutants measured by the Montreal Urban Community.

[b] Not in Montreal; measured 1986 to 1993.

Table C.1 *(continued).* Description of Monitoring Stations in Montreal, Quebec, 1984 to 1993[a]

Pollutant	Monitoring Stations	Days with Measurements	Days with Missing Values	Average of Daily Means	Range of Pearson Correlation Coefficients Between Stations
NO_2	1	2,948	705	37.01	0.33–0.57
	3	2,902	751	31.14	0.34–0.55
	12	2,972	669	41.80	0.31–0.55
	28	2,552	1,033	61.86	0.19–0.40
	29	2,718	929	33.73	0.31–0.58
	60	2,112	831	30.68	0.29–0.58
	61	3,467	186	61.87	0.27–0.44
	68	2,926	727	30.28	0.19–0.55
CO	1	3,028	625	0.53	0.26–0.60
	3	3,171	482	0.46	0.08–0.58
	12	2,450	835	0.80	0.38–0.62
	28	2,893	759	1.21	0.27–0.59
	29	2,579	977	0.74	0.28–0.57
	60	2,696	836	0.47	0.30–0.62
	61	3,103	550	1.41	0.08–0.67
	68	3,285	368	0.47	0.10–0.46
	83	50	10	5.82	0.08–0.32
	84	50	9	5.31	0.08–0.80
	85	39	16	0.67	0.10–0.80
	90	107	0		0.21–0.57

[a] PM measured by Environment Canada as part of the National Air Pollution Surveillance Program. All other pollutants measured by the Montreal Urban Community.

[b] Not in Montreal; measured 1986 to 1993.

Table C.2. Pearson Correlation Coefficients Between Different Sets of Monitoring Stations After the Exclusion of Four Stations Spatially Close to Major Expressways, Montreal, 1984 to 1993

	Mean Pearson Correlation Coefficient Between Pairs of Stations	
Pollutant	All Stations	Excluding Four Stations Located Near Major Expressways[a]
TSP	0.62	0.66
COH	0.52	0.55
Sulfate from TSP	0.69	0.65
NO_2	0.41	0.44
NO	0.58	0.60
CO	0.41	0.41
SO_2	0.44	0.44
O_3	0.71	0.73

[a] These stations are: Châteauneuf Boulevard (station number 6); Decarie Boulevard and Duncan (28); St-Michel Boulevard (44); and Lacordaire Boulevard (58).

Table C.3. Pearson Correlation Coefficients Between Total Sulfate Measured at the Sutton Monitoring Station and Various Indices of PM Measured in Montreal, 1986 to 1993

	Pearson Correlation Coefficient in Montreal		
Pollutant	Lag 0	Lag 1	Lag 2
Mean TSP	0.41	0.17	0.00
Mean COH	0.27	0.08	–0.04
Mean PM_{10}	0.54	0.28	0.05
Mean $PM_{2.5}$	0.65	0.35	0.08
Sulfate from TSP	0.74	0.48	0.12
Sulfate from PM_{10}	0.86	0.60	0.20
Sulfate from $PM_{2.5}$	0.87	0.59	0.19

Table C.4. Pearson Correlation Coefficients Among Selected Measures of Particles and Gaseous Variables, Montreal, 1984 to 1993

Variable	Correlation Coefficient
Coefficient of Haze	
Extinction	0.38
TSP	0.58
PM_{10}	0.58
$PM_{2.5}$	0.61
Sutton sulfate	0.27
Sulfate from PM_{10}	0.41
Sulfate from $PM_{2.5}$	0.40
Extinction	
TSP	0.43
PM_{10}	0.43
$PM_{2.5}$	0.54
Sutton sulfate	0.49
Sulfate from PM_{10}	0.63
Sulfate from $PM_{2.5}$	0.62
TSP	
PM_{10}	0.73
$PM_{2.5}$	0.59
Sutton sulfate	0.41
Sulfate from PM_{10}	0.54
Sulfate from $PM_{2.5}$	0.52
PM_{10}	
$PM_{2.5}$	0.87
Sutton sulfate	0.54
Sulfate from PM_{10}	0.65
Sulfate from $PM_{2.5}$	0.63
$PM_{2.5}$	
Sutton sulfate	0.65
Sulfate from PM_{10}	0.80
Sulfate from $PM_{2.5}$	0.78
Sutton Sulfate	
Sulfate from PM_{10}	0.86
Sulfate from $PM_{2.5}$	0.87
SO_2	
NO_2	0.56
NO	0.58
CO	0.65
O_3	–0.30
NO_2	
NO	0.59
CO	0.58
O_3	–0.02
NO	
CO	0.73
O_3	–0.47
CO	
O_3	–0.33

Table C.5. Pearson Correlation Coefficients Among Selected Particulate and Gaseous Variables, Montreal, 1984 to 1993

Variable	Correlation Coefficient
Coefficient of Haze	
SO_2	0.58
NO_2	0.66
NO	0.71
CO	0.69
O_3	–0.27
Extinction	
SO_2	0.29
NO_2	0.32
NO	0.19
CO	0.26
O_3	0.07
$PM_{2.5}$	
SO_2	0.52
NO_2	0.61
NO	0.41
CO	0.53
O_3	0.08
Predicted $PM_{2.5}$[a]	
SO_2	0.41
NO_2	0.60
NO	0.41
CO	0.51
O_3	0.13
Sutton Sulfate[a]	
SO_2	0.08
NO_2	0.29
NO	–0.03
CO	0.09
O_3	0.44
Sulfate from $PM_{2.5}$	
SO_2	0.17
NO_2	0.37
NO	0.04
CO	0.17
O_3	0.44
Predicted Sulfate from $PM_{2.5}$[a]	
SO_2	0.21
NO_2	0.40
NO	0.11
CO	0.23
O_3	0.36

[a] For 1986 to 1993.

Table C.6. Pearson Correlation Coefficients for Selected Weather Variables, Montreal, 1984 to 1993

Variable	Correlation Coefficient
Mean Temperature	
Dew point temperature	0.97
Change in maximum temperature from the previous day	0.13
Relative humidity	0.06
Change in barometric pressure from the previous day	–0.15
Dew Point Temperature	
Change in maximum temperature from the previous day	0.14
Relative humidity	0.27
Change in barometric pressure from the previous day	–0.23
Change in Maximum Temperature from the Previous Day	
Relative humidity	0.09
Change in barometric pressure from the previous day	–0.35

Table C.7. Results of Pilot Study to Measure Spatial Distribution of TSP and PM_{10} Around Fixed-Site Monitoring Stations, Montreal, Summer 1996

			Values from Portable Monitors ($\mu g/m^3$) and Differences from Fixed Site					
Study Area	Distance (km)	Mean Value at Fixed Station ($\mu g/m^3$)	Mean	Difference Between Means	Minimum	Difference Between Minimums	Maximum	Difference Between Maximums
TSP								
Residential	1	34.20	32.63	1.57	22.37	11.83	49.75	–15.55
	3	34.00	33.56	1.43	28.06	5.94	43.20	–9.20
Highway	1	76.14	51.45	24.69	43.75	32.39	62.80	13.34
	3	56.00	35.94	20.06	21.88	34.12	47.63	8.37
PM_{10}								
Residential	1	20.44	19.43	1.01	12.00	8.44	24.38	–3.94
	3	19.63	19.55	0.08	17.75	1.88	21.80	–2.17
Highway	1	30.50	34.15	–3.65	26.50	4.00	40.33	–9.83
	3	31.80	22.73	9.07	16.75	15.05	27.75	4.05

Table C.8. Seasonal Pattern in Measured Environmental Pollutants, Montreal, 1984 to 1993

Pollutant	Units	Number of Monitoring Stations	Means of Daily Means by Season Across Study Years				Mean
			Winter December–February	Spring March–May	Summer June–August	Autumn September–November	
TSP	$\mu g/m^3$	19	55.1	60.1	52.5	44.5	53.1
PM_{10}	$\mu g/m^3$	2	38.6	32.5	29.5	32.1	32.2
$PM_{2.5}$	$\mu g/m^3$	2	22.4	15.7	16.3	16.9	17.4
Sulfate from PM_{10}	$\mu g/m^3$	2	4.3	4.3	6.2	3.9	4.7
Sulfate from $PM_{2.5}$	$\mu g/m^3$	2	3.9	3.8	5.7	3.4	4.3
Sulfate from TSP	$\mu g/m^3$	13	4.8	3.8	4.9	3.4	4.3
Total sulfate from the Sutton monitoring station[a]	$\mu g/m^3$	1	2.6	3.2	4.4	3.1	3.3
COH	0.1 COH units per 327.8 linear meters	11	3.0	2.2	2.2	2.4	2.4
Extinction (corrected)		1	0.18	0.14	0.15	0.13	0.15
SO_2	$\mu g/m^3$	13	27.7	17.0	11.2	15.4	17.8
NO_2	$\mu g/m^3$	8	45.6	47.2	37.1	36.9	41.7
NO	$\mu g/m^3$	8	54.2	36.8	28.1	48.4	41.8
CO	ppm	12	1.1	0.7	0.6	0.8	0.8
O_3	$\mu g/m^3$	9	18.8	36.5	39.8	20.5	29.0

[a] For 1986 to 1993.

Table C.9. Sensitivity Analyses: Effect of Different Temporal Filters (LOESS[days, span=x/3,653]) on the Estimates of Excess Relative Risk Across the Interquartile Range at Lag 0, Montreal, 1984 to 1993[a]

	COH			$PM_{2.5}$			Sulfate from Sutton		
Cause of Death	31 Days	91 Days	151 Days	31 Days	91 Days	151 Days	31 Days	91 Days	151 Days
Nonaccidental deaths	1.19[b]	**1.44**[b]	1.57[b]	1.37	**0.77**	0.89	0.63[b]	**0.71**[b]	0.85[b]
Neoplasms	1.33[b]	1.26[b]	**1.15**	4.00[b]	0.75	**1.12**	1.11[b]	1.01[b]	**0.88**[b]
Lung cancer	2.56[b]	2.30[b]	**2.46**[b]	N/C	4.23	**2.77**	0.89	0.30	**0.34**
Cardiovascular diseases	0.62	**0.73**	1.01	0.28	**0.69**	0.22	0.27	**0.41**	0.72
Coronary artery disease	0.91	1.48[b]	**1.28**	1.00	0.86	**0.85**	0.62	0.64	**0.85**
Respiratory diseases	3.31[b]	**3.46**[b]	3.92[b]	0.29	**1.96**	–0.02	0.58	**0.87**	1.32
Nonmalignant digestive diseases	1.16	0.01	**0.10**	N/C	4.47	**4.50**	3.48[b]	2.87[b]	**3.00**[b]
Other nonaccidental causes	3.26[b]	**3.35**[b]	3.50[b]	0.10	**–0.39**	N/C	0.70	**0.69**	0.65
AIDS	8.26[b]	9.21[b]	**9.56**[b]	N/C	N/C	**N/C**	1.38	0.53	**0.02**
Diabetes	4.03	4.31[b]	**4.21**[b]	N/C	10.45[b]	**N/C**	3.03[b]	3.20[b]	**3.06**[b]
Renal diseases	0.69	2.03	**2.32**	N/C	N/C	**6.90**	–0.95	0.35	**0.35**
Neurological conditions	3.21	2.73	**2.79**	N/C	N/C	**–2.51**	–0.89	–1.49	**–0.61**
Accidents	0.44	1.49	**1.05**	–10.10[b]	–3.65	**N/C**	0.80	1.26	**1.02**

[a] Numbers in bold refer to the primary analyses. N/C = convergence of model not obtained.

[b] Indicates a corrected *t* value > 1.96.

Table C.10. Sensitivity Analyses: Effect of Different Weather Variables on the Estimates of Excess Relative Risk Across the Interquartile Range at Lag 0, Montreal, 1984 to 1993[a]

	COH			$PM_{2.5}$			Sulfate from Sutton (1986 to 1993)		
Cause of Death	Primary Analysis	Single Variable	None	Primary Analysis	Single Variable	None	Primary Analysis	Single Variable	None
Nonaccidental deaths	1.44b	1.46[b]	1.50[b]	0.77	0.75	1.83[b]	0.71[b]	0.93[b]	1.29[b]
Neoplasms	1.15	1.24[b]	1.40[b]	1.12	0.92	2.61	0.88[b]	1.09[b]	1.53[b]
Lung	2.46b	2.89[b]	2.79[b]	2.77	5.98[b]	5.26	0.34	1.37	1.24
Cardiovascular diseases	0.73	0.83	0.87	0.69	0.85	1.18[b]	0.41	0.88[b]	1.07[b]
Coronary artery disease	1.28	1.17	1.06	0.85	0.90	1.37	0.85	0.66	0.73
Respiratory diseases	3.46b	3.79[b]	3.50[b]	1.96	1.74	0.88[b]	0.87	1.07	1.39
Digestive diseases	0.10	0.19	0.39	4.50	5.11	5.33	3.00[b]	3.05[b]	2.60[b]
Other nonaccidental causes	3.35[b]	3.12[b]	3.16[b]	−0.39	−0.73	1.82[b]	0.69	0.69	0.94
AIDS	9.56[b]	10.36[b]	9.46[b]	N/C	N/C	N/C	0.02	0.51	0.38
Diabetes	4.21[b]	3.86	4.56[b]	N/C	9.78[b]	9.59[b]	3.06[b]	2.93[b]	2.91[b]
Renal diseases	2.32	2.26	2.08	6.90	5.90	N/C	0.35	0.25	0.10
Neurological conditions	2.79	2.68	3.16	−2.51	−2.75	−1.56	−0.61	−0.65	−0.48
Accidents	1.05	2.23	2.36	N/C	−2.99	−2.96	1.02	1.67	1.73

[a] N/C = convergence of model not obtained.

[b] Indicates a corrected t value > 1.96.

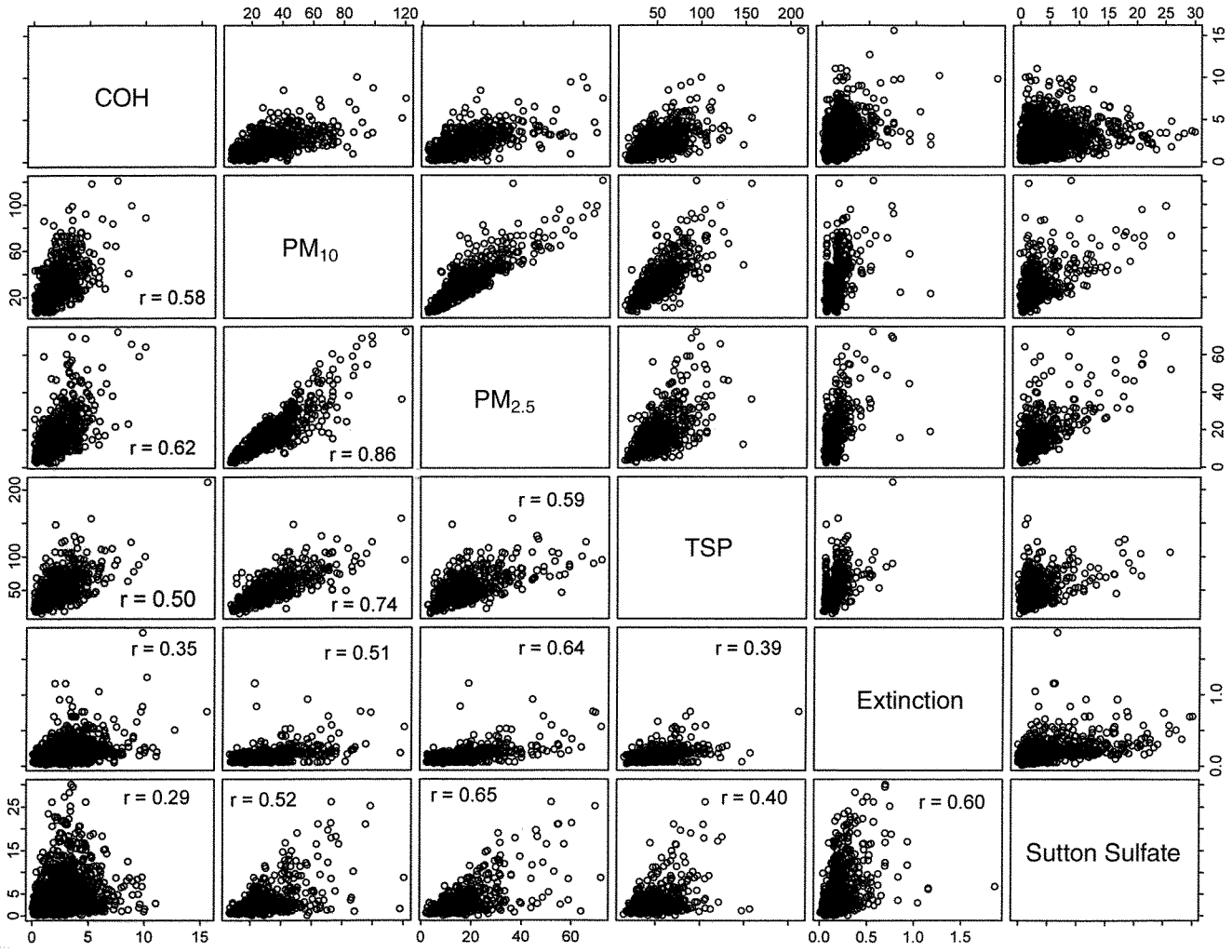

Figure C.1. Pearson correlation coefficients of selected measures of particles.

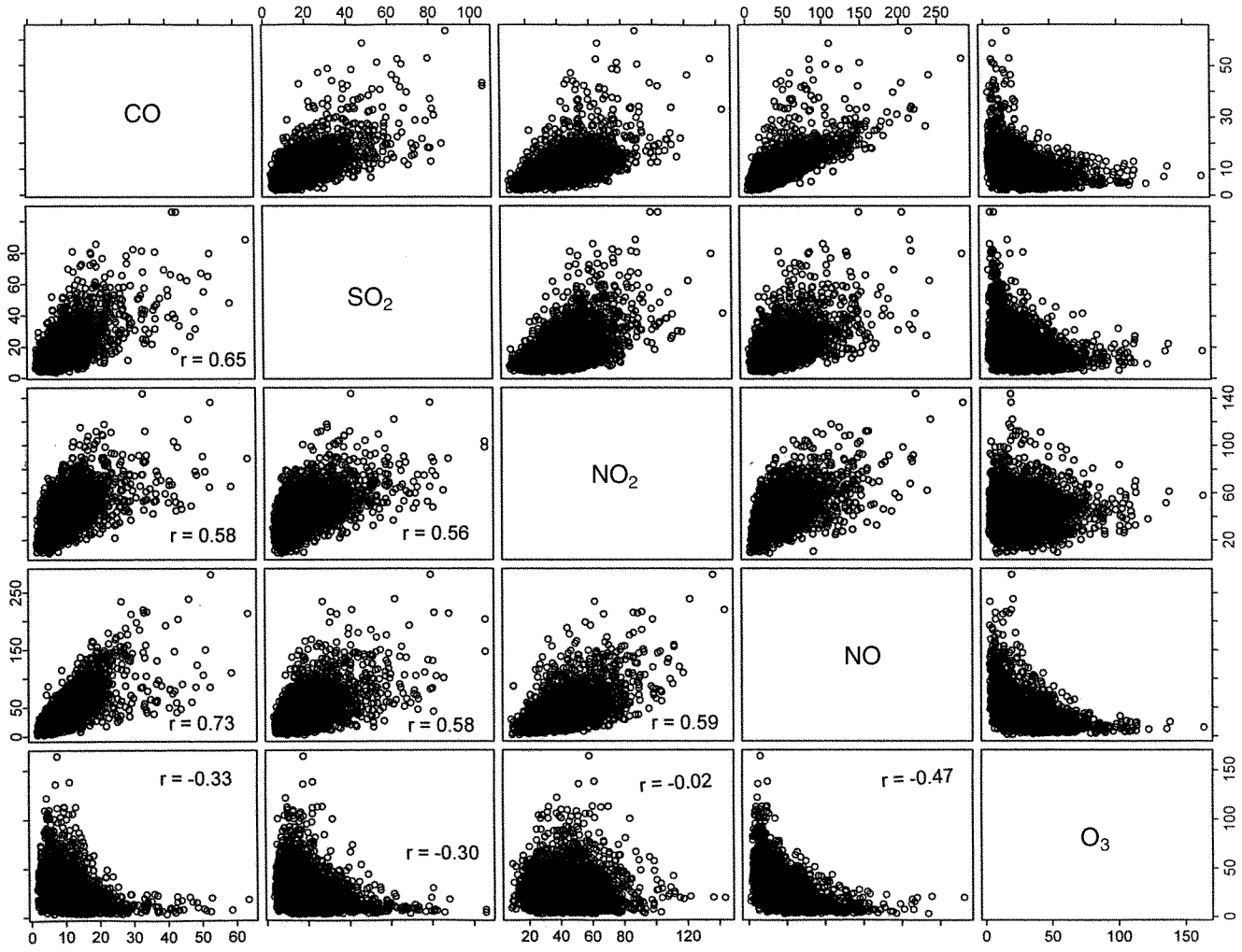

Figure C.2. Pearson correlation coefficients of gaseous pollutants.

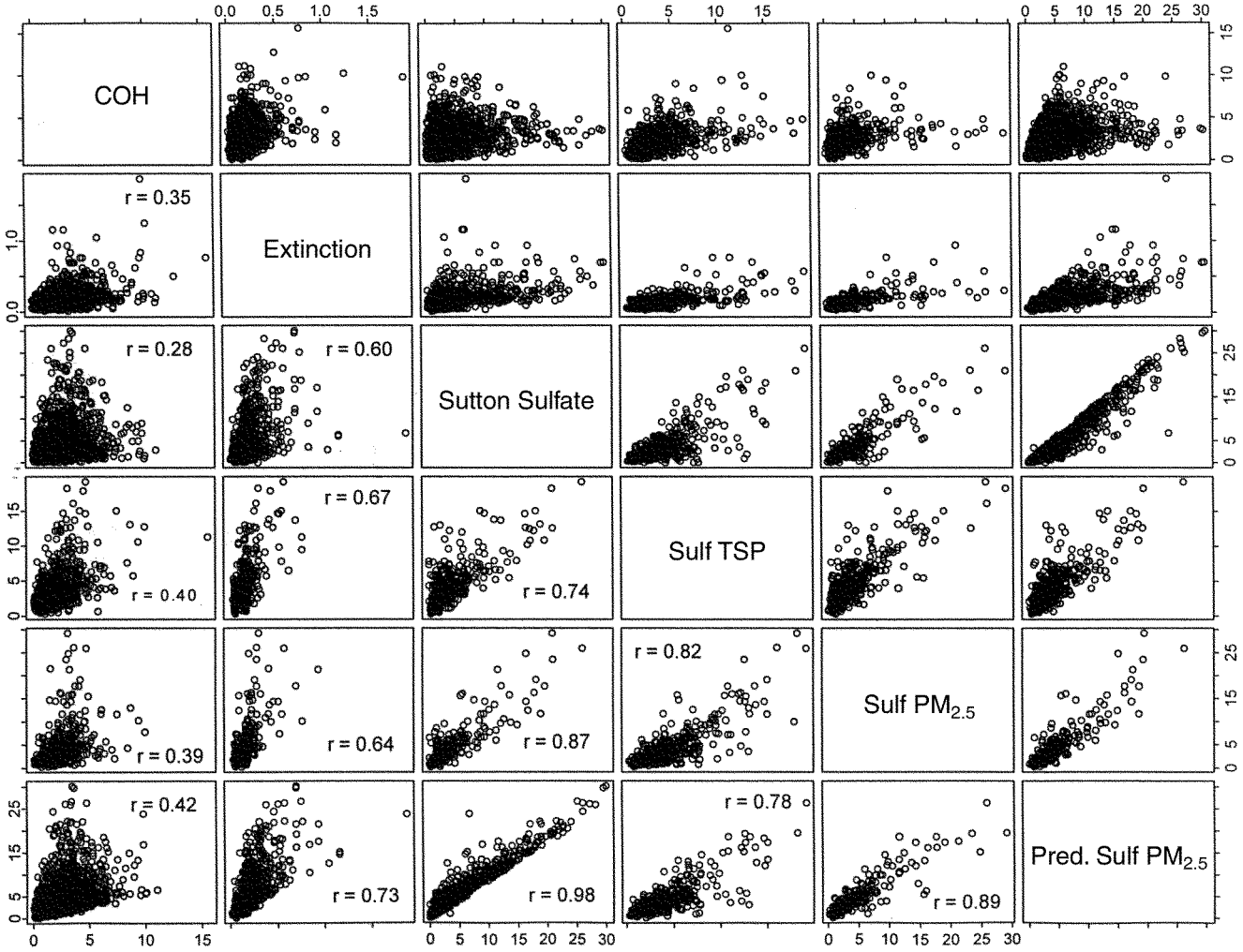

Figure C.3. Pearson correlation coefficients of selected measures of particles and sulfate.

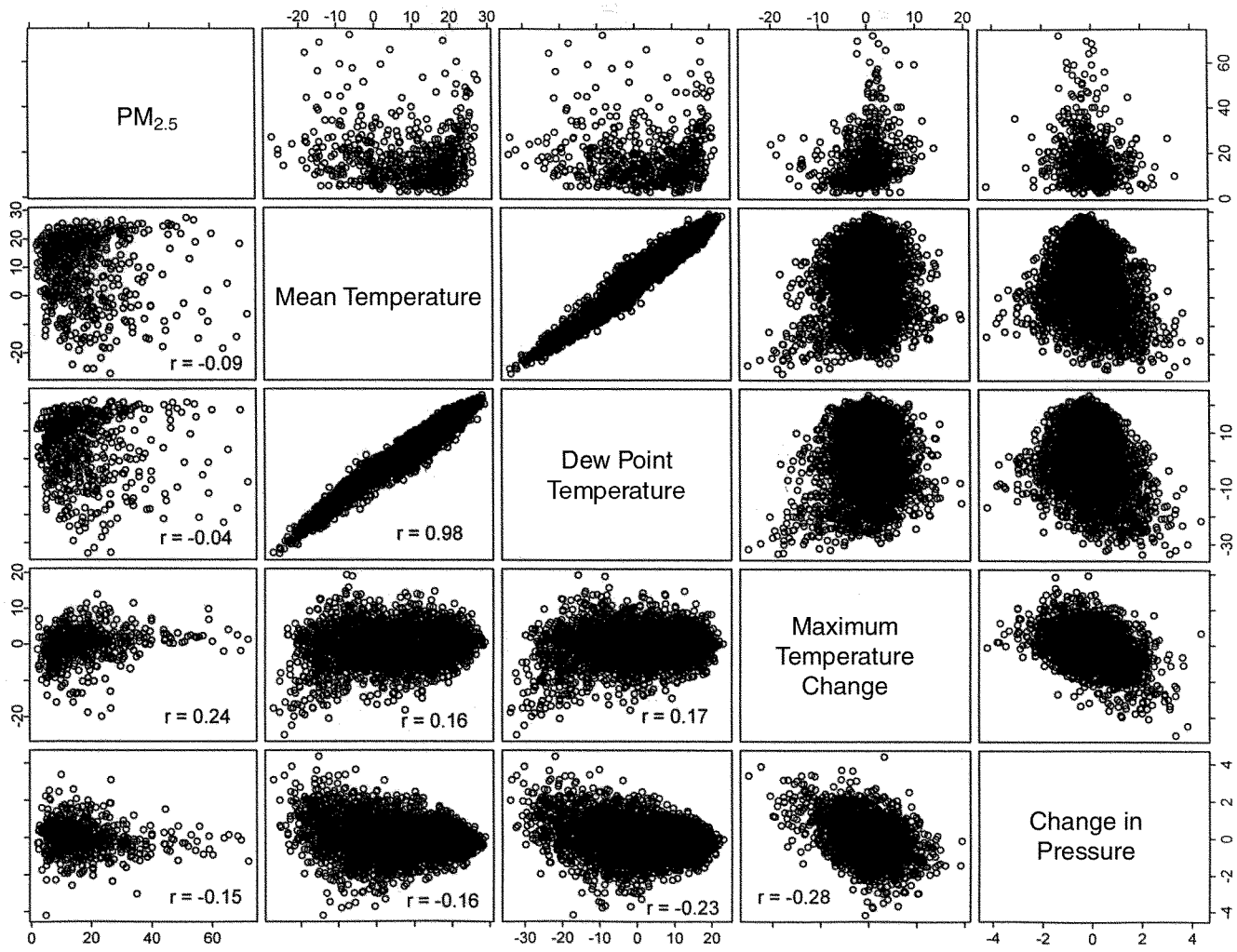

Figure C.4. Pearson correlation coefficients of $PM_{2.5}$ and selected weather variables.

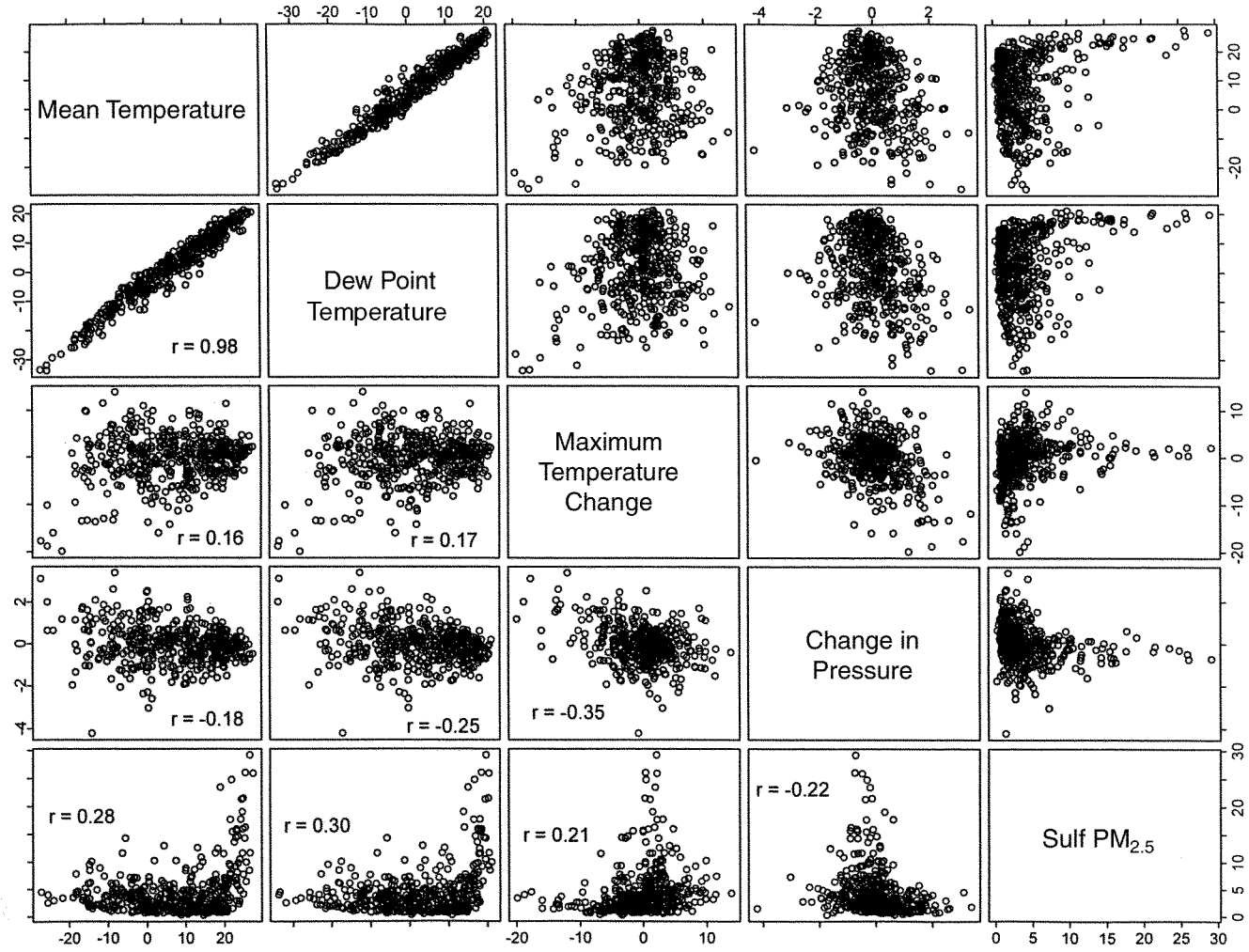

Figure C.5. Pearson correlation coefficients of sulfate from $PM_{2.5}$ and selected weather variables.

APPENDIX D. Selection of Variables for Statistical Models of Cause-Specific Mortality

Table D.1. AICs and Bartlett Statistics for Temporal Components of Cause-Specific Mortality Time Series, Montreal, 1984 to 1993

	Statistics for Temporal Filters Having Different Bandwidths[a]					
	P Value from Bartlett Statistic			AIC		
Cause of Death	0.85%	2.49%	4.13%	0.85%	2.49%	4.13%
Nonaccidental deaths	0	0.036	0	4,163.7	4,131.7	4,178.9
Neoplasms	0	0.116	0.722	3,914.2	3,798.6	3,776.9
Lung cancer	0	0.076	0.127	4,200.3	4,069.2	4,040.5
Cardiovascular diseases	0	0.180	0.139	4,078.8	3,993.6	3,995.3
Coronary artery disease	0	0.151	0.156	4,021.4	3,950.6	3,939.7
Respiratory diseases	0	0.572	0.808	4,158.8	4,081.8	4,121.5
Nonmalignant digestive diseases	0	0.201	0.781	4,336.5	4,253.7	4,230.4
Other nonaccidental causes	0	0.420	0.445	4,151.3	4,081.8	4,093.9
AIDS	0	0.799	0.653	2,742.6	2,674.7	2,671.9
Diabetes	0	0.203	0.778	4,420.9	4,317.5	4,293.2
Renal diseases	0	0.002	0.014	3,750.9	3,650.4	3,635.3
Neurological conditions	0	0.430	0.770	4,215.0	4,141.4	4,140.8
Accidents	0	0.073	0.303	4,588.8	4,441.7	4,415.3

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=x) + \text{LOESS}(\text{year})$, where i is an indicator for day and x = 31/3,653 (0.85%), 91/3,653 (2.49%), or 151/3,653 (4.13%) days.

Table D.2. Selected Statistical Characteristics of LOESS Filtered Cause-Specific Mortality Time Series, Montreal, 1984 to 1993[a]

Cause of Death	Temporal Filter (span, in %)	AIC	Bartlett Statistic	*P* Value from Bartlett Statistic	Serial Autocorrelation Coefficients				
					Lag 1	Lag 2	Lag 3	Lag 4	Lag 5
Nonaccidental deaths	2.49	4,131.7	1.415	0.036	0.04	0.00	0.00	−0.02	−0.03
Neoplasms	4.13	3,776.9	0.693	0.722	0.01	0.00	−0.02	−0.04	−0.01
Lung cancer	4.13	4,040.5	1.175	0.127	−0.01	0.03	−0.04	−0.04	0.01
Cardiovascular diseases	2.49	3,993.6	1.097	0.180	0.01	−0.03	0.02	−0.02	−0.01
Coronary artery disease	4.13	3,939.7	1.130	0.156	0.03	−0.01	0.03	0.00	−0.01
Respiratory diseases	2.49	4,081.8	0.783	0.572	−0.02	−0.02	0.00	−0.03	0.00
Nonmalignant digestive diseases	4.13	4,230.4	0.657	0.781	−0.01	0.00	−0.02	−0.02	−0.01
Other nonaccidental causes	2.49	4,081.8	0.881	0.420	−0.02	0.02	−0.01	−0.02	−0.03
AIDS	4.13	2,671.9	0.735	0.653	0.01	0.01	0.00	0.00	0.01
Diabetes	4.13	4,293.2	0.659	0.778	−0.01	−0.01	−0.01	0.00	−0.01
Renal diseases	4.13	3,635.3	1.579	0.014	−0.05	0.01	−0.01	0.03	−0.04
Neurological conditions	4.13	4,140.8	0.664	0.770	0.01	0.02	0.00	0.00	−0.01
Accidents	4.13	4,415.3	0.971	0.303	−0.01	−0.04	−0.02	−0.01	−0.03

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=x) + \text{LOESS}(\text{year})$, where i is an indicator for day and x = 0.85%, 2.49%, or 4.13%.

Table D.3. Weather Variables Included in the Cause-Specific Regression Models, Montreal, 1984–1993[a]

Cause of Death	Temporal Filter (span, in %)	Single Weather Variable[b]	AIC	Multiple Weather Variables[b]	AIC
Nonaccidental deaths	2.49	Lo(Mean $Temp_0$)	4,064.0	Lo(Mean $Temp_0$, Δ $Pressure_0$)	4,045.3
Neoplasms	4.13	Lo(Dew Point $Temp_0$)	3,756.2	Lo(Mean $Temp_0$, Δ $Pressure_0$)	3,750.6
Lung cancer	4.13	Lo(Δ Max $Temp_2$)	4,030.7	Lo(Dew Point $Temp_0$, Δ Max $Temp_2$)	4,025.2
Cardiovascular diseases	2.49	Lo(Δ $Pressure_0$)	3,967.2	Lo(Mean $Temp_1$, Δ $Pressure_0$)	3,945.6
Coronary artery disease	4.13	Lo(Δ $Pressure_0$)	3,921.2	Lo(Mean $Temp_0$) + Lo(Δ Max $Temp_2$) + Lo(Δ $Pressure_0$)	3,916.7
Respiratory diseases	2.49	Lo(Dew Point $Temp_0$)	4,073.0	Lo(Dew Point $Temp_0$, Δ Max $Temp_0$)	4,072.7
Digestive diseases	4.13	Lo(Mean $Temp_2$)	4,222.4	Lo(Mean $Temp_2$) + Lo(Δ Max $Temp_1$)	4,225.8
Other nonaccidental causes	2.49	Lo(Mean$Temp_0$)	4,072.5	Lo(Mean $Temp_0$) + Lo(Δ $Pressure_1$)	4,072.8
AIDS	4.13	Lo(Dew Point $Temp_2$)	2,661.0	Lo(Dew Point $Temp_2$) + Lo(Δ $Pressure_0$)	2,660.8
Diabetes	4.13	Lo(Mean $Temp_3$)	4,281.4	Lo(Mean $Temp_3$) + Lo(Δ $Pressure_2$)	4,284.4
Renal diseases	4.13	Lo(Δ Max $Temp_2$)	3,622.4	Lo(Δ Max $Temp_2$, Δ $Pressure_3$)	3,609.3
Neurological conditions	4.13	Lo(Mean $Temp_3$)	4,134.0	Lo(Mean $Temp_3$, Δ Max $Temp_3$)	4,134.0
Accidents	4.13	Lo(Δ $Pressure_3$)	4,405.7	Lo(Δ Max $Temp_0$, Δ $Pressure_3$)	4,408.6

[a] The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=x) + \text{LOESS}(\text{year}) + \text{weather terms}$, where i is an indicator for day and $x = 0.85\%$, 2.49%, or 4.13%.

[b] Lo = LOESS; Δ = difference; and subscripts refer to lag periods.

APPENDIX E. Synthesis of Results for Analyses of Underlying Causes of Death by Selected Indices of Ambient Air Particles

Table E.1. Synthesis of Results of Mean Percent Change in Daily Mortality from Different Measures of Particulates Evaluated at Interquartile Range, Montreal, 1984 to 1993[a]

Cause of Death	COH	Extinc–tion	TSP	PM_{10}	$PM_{2.5}$	Predicted $PM_{2.5}$	Sulfate from Sutton	Sulfate from $PM_{2.5}$	Predicted Sulfate from $PM_{2.5}$
Lag 0 Days									
Nonaccidental deaths	1.44[b]	1.05[b]	1.86[b]	1.43	0.77	1.86[b]	0.71[b]	1.86[b]	1.15[b]
≥ 65 years	1.79[b]	1.04[b]	1.98	0.77	0.21	1.91[b]	0.87[b]	1.39	1.28[b]
< 65 years	0.57	1.16	1.59	3.66[b]	2.53	1.83[b]	0.34	3.20[b]	0.88
Neoplasms	1.15	1.16[b]	1.53	1.44	1.12	1.55[b]	0.88[b]	2.82[b]	1.27[b]
Lung cancer	2.46[b]	1.71	6.13[b]	2.34	2.77	1.56	0.34	0.46	0.81
Cardiovascular diseases	0.73	0.86	1.86	1.54	0.69	0.97	0.41	2.07	0.62
Coronary artery disease	1.28	1.10	2.58	0.13	0.85	1.04	0.85	1.01	0.89
Respiratory diseases	3.46[b]	0.95	1.61	3.32	1.96	3.58[b]	0.87	–2.88	1.75
≥ 65 years	4.06[b]	0.99	1.83	3.16	2.11	4.24[b]	1.28	–3.20	2.33[b]
Nonmalignant digestive diseases	0.10	2.71	9.35[b]	N/C	4.50	4.47[b]	3.00[b]	8.65[b]	3.79[b]
Accidents	1.05	0.07	–4.14	–6.46	N/C	1.08	1.02	–0.34	1.24
Other nonaccidental causes	3.35[b]	1.42	1.27	–0.18	–0.39	3.01[b]	0.69	–0.94	1.26
AIDS	9.56[b]	4.02	1.31	N/C	N/C	4.88	0.02	N/C	1.82
Diabetes	4.21[b]	4.33[b]	0.99	N/C	N/C	5.48[b]	3.06[b]	N/C	3.77[b]
Renal diseases	2.32	0.57	5.71	–2.86	6.90	–0.12	0.35	5.76	–0.12
Neurological conditions	2.79	0.60	2.29	N/C	–2.51	1.51	–0.61	N/C	–0.12
Lag 1 Day									
Nonaccidental deaths	1.12[b]	0.86[b]	1.04	0.80	1.45	1.48[b]	0.95[b]	1.62[b]	1.15[b]
≥ 65 years	1.69[b]	1.05[b]	2.29[b]	1.65	1.63	1.75[b]	1.06[b]	2.10[b]	1.34[b]
< 65 years	–0.42	0.29	–2.92	–1.95	0.78	0.93	0.67	0.22	0.72
Neoplasms	1.17	0.81	–0.26	–2.96	–0.35	1.15	0.59	–1.28	0.82
Lung cancer	0.65	–0.42	6.17	3.01	3.14	0.71	0.60	0.54	0.76
Cardiovascular diseases	0.28	0.60	–0.39	1.92	1.68	0.77	0.97[b]	2.32[b]	0.93[b]
Coronary artery disease	0.46	1.25[b]	–0.25	2.68	2.80	1.17	1.21[b]	1.99	1.29[b]
Respiratory diseases	3.69[b]	2.32[b]	3.70	1.50	5.80[b]	4.80[b]	3.22[b]	6.18[b]	3.51[b]
≥ 65 years	4.65[b]	2.89[b]	5.59	3.05	6.35[b]	6.01[b]	3.62[b]	6.87[b]	4.20[b]
Nonmalignant digestive diseases	–0.77	1.29	2.20	1.29	–3.18	0.88	–0.63	N/C	0.22
Accidents	3.56[b]	–0.19	–5.09	3.18	3.01	3.06	1.37	N/C	1.90
Other nonaccidental causes	2.91[b]	0.89	3.55	4.75	3.66	2.76[b]	1.16	2.51	1.74[b]
AIDS	0.20	–4.17	–5.93	N/C	N/C	0.09	0.95	4.36	–0.26
Diabetes	5.99[b]	2.93	5.92	13.20[b]	12.03[b]	5.94[b]	2.39	7.71	3.79[b]
Renal diseases	0.52	0.40	–7.69	–6.94	–11.19	–0.96	–2.16	N/C	–1.52
Neurological conditions	0.76	–2.04	12.35[b]	9.75[b]	N/C	–0.03	0.38	N/C	0.01

(Table continues next page)

[a] The Sutton sulfate data were from 1986 to 1993 only. The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=x) + \text{LOESS}(\text{year}) + \text{multiple weather variables} + \beta \times (\text{pollutant})$, where i is an indicator for day and x is the selected span (percent) (Table D.2). See Table D.3 for the included weather variables. N/C = convergence of model not obtained.

[b] Corrected t value > 1.96.

Table E.1 (*continued*). Synthesis of Results of Mean Percent Change in Daily Mortality from Different Measures of Particulates Evaluated at Interquartile Range, Montreal, 1984 to 1993[a]

Cause of Death	COH	Extinc–tion	TSP	PM_{10}	$PM_{2.5}$	Predicted $PM_{2.5}$	Sulfate from Sutton	Sulfate from $PM_{2.5}$	Predicted Sulfate from $PM_{2.5}$
3-Day Mean									
Nonaccidental deaths	1.98[b]	1.67[b]				2.17[b]	1.29[b]		1.59[b]
≥ 65 years	2.57[b]	1.96[b]				2.68[b]	1.77[b]		2.11[b]
< 65 years	0.30	0.88				1.03	0.04		0.27
Neoplasms	2.34[b]	2.01[b]				1.40	0.75		0.97
Lung cancer	3.05[b]	2.19				1.82	0.39		1.11
Cardiovascular diseases	0.19	0.72				1.31	1.31[b]		1.30[b]
Coronary artery disease	0.94	1.89[b]				1.68	1.50[b]		1.62[b]
Respiratory diseases	5.98[b]	4.03[b]				7.73[b]	3.86[b]		5.24[b]
≥ 65 years	6.90[b]	4.33[b]				9.03[b]	4.64[b]		6.25[b]
Nonmalignant digestive diseases	−1.28	1.81				1.90	0.67		1.29
Neurological conditions	1.98	0.07				0.66	0.12		0.35
Other nonaccidental causes	5.14[b]	2.63[b]				3.93[b]	2.04[b]		2.49[b]
AIDS	7.43	2.92				3.40	0.51		0.99
Diabetes	7.50[b]	5.52[b]				7.59[b]	4.48[b]		4.98[b]
Renal diseases	0.25	−1.30				−1.66	−0.10		−0.55
Accidents	3.38	−1.37				2.04	1.73		1.69

[a] The Sutton sulfate data were from 1986 to 1993 only. The statistical model was $E[\log(y_i)] = \alpha + \text{LOESS}(i, \text{span}=x) + \text{LOESS}(\text{year}) + \text{multiple weather variables} + \beta \times (\text{pollutant})$, where i is an indicator for day and x is the selected span (percent) (Table D.2). See Table D.3 for the included weather variables. N/C = convergence of model not obtained.

[b] Corrected t value > 1.96.

APPENDIX F. Characteristics of Morbidity Groups

Tables F.1 and F.2 show the ICD-9 codes used to define the cardiovascular and respiratory diseases, respectively. Table F.6 shows the distribution of the diagnoses that contributed to each group.

ACCURACY OF DISEASE GROUPS

It was not possible to independently validate these indicators through a direct comparison with physician and hospital charts. We were, however, able to carry out a reliability study for subjects who were hospitalized prior to death. This substudy used hospital discharge data from the Quebec Hospitalization Discharge Database (Bourdages 1987). Since 1981, all acute care hospitals in Quebec have been required to report to the system; nursing homes and similar institutions do not report. Each hospital is responsible for abstracting and verifying its own data.

This substudy was limited to deceased and control subjects who were hospitalized between 1990 and 1993. This time restriction arose because there was no identifying information on the hospital discharge file before 1990, when QHIP numbers were added, to individual records on the database. We thus linked the subset of subjects who were hospitalized in Quebec between 1990 and 1993 (described in Part 1), and we compared our indicators of disease group, defined for the nested intervals of one year, six months, and two months before death, to diagnoses listed on the hospital discharge database for the same periods of time.

The hospital discharge database contained information on conditions that contributed to the hospital stay. Such conditions were coded to the ICD-9 by trained nosologists in each hospital, and previous conditions that did not affect length of stay should not have been recorded. Studies of cerebrovascular diseases (Mayo et al 1993) and respiratory conditions (Delfino et al 1993) have found excellent agreement between hospital charts and the hospital discharge database.

We declared an agreement if any of the conditions that contributed to the hospital stay matched those used in the definition of the morbidity indices. We report simple indices of agreement that are based on the cross-classification of the presence or absence of the condition on the hospital discharge record and attributed by our indicators of disease group. Of the many statistical indices available for summarizing pairwise agreement, we chose two for presentation. The first index was simply the total percentage of subjects in which we observed perfect agreement (absence and presence; this statistic is referred to as percent perfect agreement or crude agreement, p_0). The second index of agreement used was Cohen kappa (κ) (Fleiss 1981). Kappa is calculated by subtracting the agreement expected by chance (p_e) from the percent perfect agreement ($p_0 - p_e$) and then dividing the result by the maximum excess expected agreement ($1 - p_e$). We calculated estimates of variance using the large sample formula, and calculated 95% CIs assuming that κ was distributed normally.

When κ is zero, the degree of observed agreement is equal to that expected by chance ($p_0 = p_e$). The maximum

Table F.1. Diagnoses Used in Defining Indicators of Cardiovascular Disease Groups

ICD-9 Code	Description
Hypertension (High BP)	
401	Essential hypertension
402	Hypertensive heart disease
403	Hypertensive renal disease
404	Hypertensive renal and heart disease
405	Secondary hypertension
Congestive heart failure (CHF)	
428	Heart failure (includes: congestive, left heart, unspecified)
Acute coronary artery disease (Acute MI)	
410	Acute myocardial infarction
411	Other acute and subacute forms of ischemic heart disease
Chronic coronary artery diseases (CCAD)	
412	Old myocardial infarction (Old MI)
413	Angina pectoris (Angina)
414	Other forms of chronic ischemic heart disease
Cerebrovascular diseases (Stroke)	
430	Subarachnoid hemorrhage
431	Intracerebral hemorrhage
432	Other and unspecified intracranial hemorrhage
433	Occlusion and stenosis of precerebral arteries
434	Occlusion of cerebral arteries
435	Transient cerebral ischemia
436	Acute, but ill-defined, cerebrovascular disease
437	Other and ill-defined cerebrovascular disease
438	Late effects of cerebrovascular disease
Chest pain	
786.5	Chest pain
Chronic rheumatic heart diseases (CRHD)	
393	Chronic rheumatic pericarditis
394	Diseases of the mitral valve
395	Diseases of the aortic valve
396	Diseases of mitral and aortic valves

Table F.2. Diagnoses Used in Defining Indicators of Respiratory Disease Groups

ICD-9 code	Description
Chronic upper respiratory (CUR)	
472	Chronic pharyngitis and nasopharyngitis
473	Chronic sinusitis
474	Chronic disease of tonsils and adenoids
475	Peritonsillar abscess
476	Chronic laryngitis and laryngotracheitis
477	Allergic rhinitis
478	Other diseases of upper respiratory tract
012.3	Tuberculous laryngitis
Chronic lower respiratory (CLR)	
490	Bronchitis, not specified as acute or chronic
491	Chronic bronchitis
492	Emphysema
493	Asthma
494	Bronchiectasis
495	Extrinsic allergic alveolitis
496	Chronic airway obstruction, NEC[a]
500–508	Pneumoconioses
515	Postinflammatory pulmonary fibrosis
516	Other alveolar and parietoalveolar pneumonopathy
517.2	Lung involvement in systemic sclerosis
517.8	Lung involvement in other diseases classified elsewhere
518.1–518.2	Interstitial and compensatory emphysema
518.3	Pulmonary eosinophilia
518.8	Other diseases of lung, NEC
519.1	Other diseases of trachea and bronchus, NEC
519.2	Mediastinitis
519.3	Other diseases of mediastinum, NEC
519.8	Other diseases of respiratory system, NEC
519.9	Unspecified disease of respiratory system
010	Primary tuberculous infection
011	Pulmonary tuberculosis
012.0	Tuberculous pleurisy
012.1	Tuberculosis of intrathoracic lymph nodes
012.8	Other specified respiratory tuberculosis
018	Miliary tuberculosis
510	Empyema
511	Pleurisy
514	Pulmonary congestion and hypostasis

(Table continues next column)

Table F.2 *(continued)*. Diagnoses Used in Defining Indicators of Respiratory Disease Groups

ICD-9 code	Description
Acute upper respiratory (AUR)	
460	Acute nasopharyngitis
461	Acute sinusitis
462	Acute pharyngitis
463	Acute tonsillitis
464	Acute laryngitis and tracheitis
465	Acute upper respiratory infections of multiple or unspecified sites
Acute lower respiratory (ALR)	
466	Acute bronchitis and bronchiolitis
480–486	Various forms of pneumonia
487	Influenza
512	Pneumothorax
513	Abscess of lung and mediastinum
517.1	Rheumatic pneumonia
518.0	Pulmonary collapse
518.4	Acute edema of lung, unspecified
518.5	Pulmonary insufficiency following trauma and surgery
519.0	Tracheostomy complication
Airways disease (AD)	
490	Bronchitis, not specific as acute or chronic
491	Chronic bronchitis
492	Emphysema
493	Asthma
494	Bronchiectasis
495	Extrinsic allergic alveolitis
496	Chronic airway obstruction, NEC
500–508	Pneumoconioses
518.1–518.2	Interstitial and compensatory emphysema
518.3	Pulmonary eosinophilia
518.8	Other diseases of lung, NEC
519.1	Other diseases of trachea and bronchus, NEC
519.2	Mediastinitis
519.3	Other diseases of mediastinum, NEC
519.8	Other diseases of respiratory system, NEC
519.9	Unspecified disease of respiratory system

[a] NEC = not elsewhere classified.

Table F.3. List of Procedures Used to Define Indicators of Disease Groups for Cardiovascular Diseases, Respiratory Conditions, and Cancer

	Number of Procedure Codes
Cardiovascular Indices	
Chronic coronary artery disease	
Coronary catheterization	5
Coronary grafts and bypass	
Arteriography	
Coronography	
Arterial angiography	
Stress tests	7
Ischemic exercise tests	
Treadmill / stationary bicycle ergometric tests with ECG monitoring	
Whalen / Makhoul stress tests	
Coronary artery disease (chronic and acute)	
Bypass	12
Thrombo-endarterectomy	
Revascularization of myocardium	
Respiratory Indices	
Airways disease	
Pulmonary function tests, with or without bronchodilators	23
Standard pulmonary function tests	
Bronchospirometry	
Histamine / metacholine challenge tests	
Jones tests	
Cancer	113
Various chemotherapeutic services (from the billing system)	
Surgical removal of tumors, including cryosurgery	

value that κ can attain is unity (perfect agreement) and its minimum value is $-1/(1 - p_e)$. Values of κ below 0.4 have, arbitrarily, been characterized as "poor" agreement; those between 0.4 and 0.75 understood as "fair to good," and values greater than 0.75 are said to represent "excellent" agreement (Fleiss 1981).

Tables F.7, F.8, and F.9 show, for deceased subjects, the analyses of agreement comparing the indices of disease group to reasons for hospitalization (1990–1993) for the three time intervals before death. We found 39,304 deceased subjects who were hospitalized in Quebec two months before they died, representing about 70% of the deaths that occurred in this three-year period. For the one-year period before death, about 99% of subjects had been hospitalized.

We noted little variation in agreement according to time before death. For conditions that usually require hospitalization (acute coronary artery disease, stroke, and cancer), we generally found high levels of crude agreement, and the chance-corrected κ values indicated "good" to "excellent" levels of agreement. We observed slightly lower levels of agreement for conditions that do not necessarily require hospitalization (congestive heart failure, hypertension, and airways disease). Interestingly, high crude agreement was found for some conditions that do not usually require hospitalization, such as upper respiratory disease. The fact that physicians decided to record these latter conditions in their billings and the fact that they contributed to a hospital stay suggests that these cases may have been severe. (The aberrantly low values of κ for this and other indices with high percent perfect agreement were due to small numbers in one or more cells of the contingency table that made expected and crude agreement almost equal.)

RISK OF DEATH INDEPENDENT OF THE EFFECTS OF AIR POLLUTION

We show in Table F.11 results of the case-control analysis comparing the deceased group to the control population according to different disease groups. We included in the regression models the set of morbidity indices described above as well as other prevalent diseases usually associated with mortality (Table F.12). For these other diseases, we used only diagnoses listed by physicians in their billings, excluding any information regarding pharmaceuticals or medical services and procedures. Multivariate unconditional logistic regression models (Breslow and Day 1980), adjusting for age, gender, and other indicators of disease group, were applied to estimate odds ratios and associated 95% confidence intervals (CI).

Table F.11 shows that the odds ratios increased with decreasing time interval before the reference date and that subjects at highest risk were those who had cancer, renal disease, acute coronary artery disease, congestive heart failure, cerebrovascular disease, and acute lower respiratory disease. Not having any interaction with the health care system before the reference date ("no billings") conferred 2- to 3.5-fold increase in odds of death.

Table F.4. List of Drugs Used in the Definitions of the Respiratory and Cardiovascular Indices[a]

	Dates Used
Respiratory Indices	
Airways Disease: Bronchodilators (beta-agonists, etc), anticholinergics, theophylline	
Aminophylline	1979–1993
Bufylline	1979–1982
Dyphylline	1979–1984
Fenoterol (bromhydrate)	1979–1993
Hydroxyethyltheophylline	1979
Ipratropium (bromure)	1983–1993
Isoproterenol (chlorhydrate)	1979–1993
Isoproterenol (chlorhydrate)/phenylephrine (bitartrate)	1979–1992
Isoproterenol (chlorhydrate)/phenylephrine (chlorhydrate)	1979–1991
Isoproterenol (sulfate)	1979–1993
Orciprenaline (sulfate)	1979–1993
Oxtriphylline	1983–1993
Procaterol hemihydrate (chlorhydrate)	1991–1993
Pseudo-ephedrine (chlorhydrate)	1979–1981
Salbutamol	1979–1993
Salbutamol (sulfate)	1979–1993
Terbutaline (sulfate de)	1979–1993
Theophyllinate (choline)	1979–1983
Theophylline	1979–1993
Theophylline (calcium aminoacetate)	1979–1993
Theophylline (sodium aminoacetate)	1979–1985
Airways Disease: Systemic and inhaled corticosteroids, sodium chromoglycate (chromolyn)	
Beclomethasone (dipropionate)	1979–1993
Betamethasone	1979–1993
Betamethasone (acetate)	1979–1985
Betamethasone (benzoate)	1979–1993
Betamethasone (dipropionate)	1979–1993
Betamethasone (dipropionate)/salicylic (acid)	1983–1990
Betamethasone (phosphate disodium)	1979–1985
Betamethasone (phosphate sodium)	1986–1993
Betamethasone (valérate)	1979–1993
Budesonide	1989–1993
Cortisone (acetate)	1979–1993
Cromoglycate disodium	1979–1988
Cromoglycate sodium	1979–1993
Desoxycorticosterone	1979–1980
Dexamethasone	1979–1993
Dexamethasone (phosphate sodium)	1979–1993
Dexamethasone (sodium phosphate)	1979–1993
Dexamethasone (tebutate)	1979–1987
Flunisolide	1979–1993
Hydrocortisone	1979–1993
Hydrocortisone (acetate)	1979–1993
Hydrocortisone (acetate)/urea	1982–1993
Hydrocortisone (acetate)/zinc oxide	1979

(Table continues next page)

[a] Names of drugs are translated from the French by the first author.

Table F.4 (*continued*). List of Drugs Used in the Definitions of the Respiratory and Cardiovascular Indices[a]

	Dates Used
Airways Disease: Systemic and inhaled corticosteroids, sodium chromoglycate (chromolyn) ***(continued)***	
Hydrocortisone (succinate sodium)	1979–1993
Hydrocortisone (valerate)	1979–1993
Hydrocortisone/atropine (sulfate)	1979–1990
Hydrocortisone/salicylic (acid)/sulfur (colloidal)	1979–1981
Ketotifene (fumarate)	1991–1993
Methylprednisolone	1979–1993
Methylprednisolone (acetate)	1979–1993
Methylprednisolone (acetate)/lidocaine (chlorhydrate)	1979–1993
Methylprednisolone (disodium phosphate)	1979–1988
Methylprednisolone (sodium succinate)	1979–1993
Phosphate sodium betamethasone	1986
Prednisolone	1979–1993
Prednisolone (acetate)	1979–1993
Prednisolone (acetate)/atropine (sulfate)	1979–1993
Prednisolone (phosphate sodium)	1979–1993
Prednisone	1979–1993
Triamcinolone	1979–1993
Triamcinolone (acetonide)	1979–1993
Triamcinolone (diacetate)	1979–1993
Triamcinolone (hexacetonide)	1979–1993
Cardiovascular Indices	
Hypertension	
Acebutol (chlorhydrate)	1987–1993
Amiloride (chlorhydrate)/hydrochlorothiazide	1981–1993
Amlodipine (besylate)	1993
Atenolol	1984–1993
Bendroflumethiazide	1979–1993
Benzthiazide	1979–1981
Captopril	1982–1993
Chlorthalidone	1979–1993
Chlorthiazide	1979–1987
Clonidine (chlorhydrate)	1979–1993
Diltiazem (chlorhydrate)	1983–1993
Enalapril	1988–1993
Enalapril hydrochlorothiazide (maleate)	1991–1993
Felodipine	1992–1993
Hydralazine (chlorhydrate)	1979–1993
Hydrochlorothiazide	1979–1993
Indapamide (hemihydrate)	1983–1993
Labetalol (chlorhydrate)	1984–1993
Lisinopril	1991–1993
Lisinopril/hydrochlorothiazide	1993
Methazolamide	1979
Methyldopa	1979–1993
Metolazone	1979–1993

(Table continues next page)

[a] Names of drugs are translated from the French by the first author.

Table F.4 (*continued*). List of Drugs Used in the Definitions of the Respiratory and Cardiovascular Indices[a]

	Dates Used
Hypertension (*continued*)	
Metoprolol (tartar)	1979–1993
Minoxidil	1981–1993
Nadolol	1980–1993
Nicardipine (chlorhydrate)	1991–1993
Nifedipine	1983–1993
Oxprenolol (chlorhydrate)	1981–1993
Pindolol	1979–1993
Pindolol/hydrochlorothiazide	1986–1993
Prazosin (chlorhydrate)	1979–1993
Propanolol (chlorhydrate)	1979–1993
Quinapril (chlorhydrate)	1993
Rauwolfia serpentina	1979–1987
Reserpine	1979–1993
Sotalol (chlorhydrate)	1985–1993
Spironolactone/hydrochlorothiazide	1979–1993
Timolol (maleate)	1979–1993
Triamterene/hydrochlorothiazide	1979–1993
Verapamil (chlorhydrate)	1980–1981 1983–1993
Congestive Heart Failure	
Amiloride (chlorhydrate)/hydrochlorothiazide	1981–1993
Benzthiazide	1979–1981
Chlorthalidone	1979–1993
Chlorthiazide	1979–1987
Hydrochlorothiazide	1979–1993
Indapamide (hemihydrate)	1983–1993
Methazolamide	1979
Metolazone	1979–1993
Spironolactone/hydrochlorothiazide	1979–1993
Triamterene/hydrochlorothiazide	1979–1993
Chronic Coronary Artery Disease	
Dinitrate isosorbite	1979–1993
Trinitrate glyceryal	1979–1993
Trinitrate glyceryal (stabilized)	1983–1993

[a] Names of drugs are translated from the French by the first author.

Table F.5. Distribution of the Number of Different Drug Identification Numbers (DINs) Used in the Making of the Cardiovascular and Respiratory Disease Groups

Drug Name	Number of Different DINs
Aminophylline	31
Oxtriphylline	21
Theophylline	113
Epinephrine (bitartrate)	7
Epinephrine hydrochloride (racemic)	4
Fenoterol hydrobromide	6
Isoproterenol hydrochloride	7
Orciprenaline sulfate	7
Procaterol hydrochloride hemihydrate	1
Salbutamol	6
Salbutamol sulfate	52
Terbutalin sulfate	7
Beclomethasone dipropionate	49
Budesonide	14
Flunisolide	4
Triamcinolone	6
Acebutolol hydrochloride	27
Atenolol	18
Metoprolol tartrate	23
Nadolol	15
Pindolol	21
Propanolol hydrochloride	45
Sotalol hydrochloride	16
Labetalol hydrochloride	6
Oxprenolol hydrochloride	5
Pindolol hydrochlorothiazide	2
Timolol maleate	36
Nifedipine	28
Diltiazem hydrochloride	39
Verapamil hydrochloride	26
Nicardipine hydrochloride	2
Amlodipine besylate	2
Felodipine	9
Chlorthalidone	14
Furosemide	47
Hydrochlorothiazide	48
Indapamide (hemihydrate)	8
Metolazone	6
Bendroflumethiazide	2
Sodium ethacrynate	1
Ethacrynic acid	1
Methyclothiazide	2
Amiloride hydrochloride	1
Amiloride hydrochloride hydrochlorothiazide	6

(Table continues next column)

Table F.5 (*continued*). Distribution of the Number of Different Drug Identification Numbers (DINs) Used in the Making of the Cardiovascular and Respiratory Disease Groups

Drug Name	Number of Different DINs
Spironolactone	8
Spironolactone/hydrochlorothiazide	4
Triamterene	4
Triamterene/hydrochlorothiazide	7
Isosorbide dinitrate	21
Glyceryl trinitrate	42
Glyceryl trinitrate (stabilized)	5
Captopril	29
Enalapril maleate	8
Enalapril maleate hydrochlorothiazide	1
Lisinopril	10
Lisinopril hydrochlorothiazide	8
Fosinopril sodic	2
Quinapril hydrochloride	4
Cilazapril	3
Benazepril	3

Table F.6. Number of Subjects Having at Least One Diagnosis Used to Define Respiratory, Cardiovascular, and Cancer Indices

Diagnosis	1 Year Prior to Death		6 Months Prior to Death		2 Months Prior to Death	
	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects
Chronic Upper Respiratory						
Chronic pharyngitis and nasopharyngitis	332	714	164	368	56	140
Chronic sinusitis	283	559	134	288	66	101
Chronic disease of tonsils and adenoids	17	56	14	37	5	16
Peritonsillar abscess	3	15	0	12	0	5
Chronic laryngitis and laryngotracheitis	38	171	22	104	7	48
Allergic rhinitis	363	499	199	240	59	82
Other diseases of upper respiratory tract	73	872	40	551	12	285
Tuberculous laryngitis	1	0	0	0	0	0
Acute Upper Respiratory						
Acute nasopharyngitis	314	551	180	286	90	103
Acute sinusitis	125	208	53	120	18	44
Acute pharyngitis	593	1,361	297	693	116	256
Acute tonsillitis	151	624	87	430	39	261
Acute laryngitis and tracheitis	259	750	128	421	59	164
Acute upper respiratory infections of multiple or unspecified sites	1,321	2,810	707	1,593	315	704
Acute Lower Respiratory						
Acute bronchitis and bronchiolitis	1,089	3,475	552	2,104	251	1,003
Viral pneumonia	14	181	7	131	4	85
Pneumococcal pneumonia (*Streptococcus pneumoniae* pneumonia)	41	837	20	679	8	535
Other bacterial pneumonia	58	967	32	770	12	582
Pneumonia due to other specified organism	1	51	1	36	1	27
Pneumonia in infectious diseases classified elsewhere	4	26	2	15	1	5
Bronchopneumonia, organism unspecified	125	2,892	57	2,361	24	1,784
Pneumonia, organism unspecified	641	13,331	315	10,995	148	8,265
Influenza	852	2,434	420	1,320	210	545
Pneumothorax	8	571	4	460	2	341
Abscess of lung and mediastinum	2	113	1	85	1	59
Rheumatic pneumonia	0	0	0	0	0	0
Pulmonary collapse	22	555	14	433	6	316
Acute edema of lung, unspecified	178	6,666	94	5,628	38	4,272
Pulmonary insufficiency following trauma and surgery	15	1,162	5	980	1	779
Tracheostomy complication	1	42	1	31	0	19

(Table continues next page)

[a] NEC = not elsewhere classified.

Table F.6 (*continued*). Number of Subjects Having at Least One Diagnosis Used to Define Respiratory, Cardiovascular, and Cancer Indices

Diagnosis	1 Year Prior to Death		6 Months Prior to Death		2 Months Prior to Death	
	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects
Airways Disease						
Bronchitis, not specified as acute or chronic	960	4,672	498	2,984	225	1,527
Chronic bronchitis	849	9,545	509	7,411	241	5,083
Emphysema	385	4,512	239	3,375	117	2,147
Asthma	871	5,380	571	3,867	268	2,260
Bronchiectasis	52	474	34	357	18	206
Extrinsic allergic alveolitis	3	46	2	40	1	23
Chronic airway obstruction, NEC[a]	680	7,367	408	5,554	185	3,679
Coal workers' pneumoconiosis	2	8	0	6	0	3
Asbestosis	3	60	2	48	0	25
Pneumoconiosis due to other silica or silicates	5	70	4	56	2	34
Pneumoconiosis due to other inorganic dust	1	10	1	4	1	3
Pneumonopathy due to inhalation of other dust	1	7	1	5	1	5
Pneumoconiosis, unspecified	2	27	2	18	1	8
Respiratory conditions due to chemical fumes and vapors	3	35	2	25	0	16
Pneumonitis due to solids and liquids	2	98	1	83	1	64
Respiratory conditions due to other and unspecified external agents	1	27	1	21	0	15
Interstitial emphysema	2	48	0	32	0	24
Compensatory emphysema	0	2	0	2	0	1
Pulmonary eosinophilia	0	55	0	39	0	25
Other diseases of lung, NEC	207	2,766	120	2,075	62	1,352
Other diseases of trachea and bronchus, NEC	39	540	26	389	7	247
Mediastinitis	2	19	1	14	0	13
Other diseases of mediastinum, NEC	0	8	0	7	0	6
Other diseases of respiratory system, NEC	104	353	61	197	25	94
Unspecified disease of respiratory system	32	382	20	291	7	187
Hypertension						
Essential hypertension	5,739	14,470	4,007	9,009	2,023	4,148
Hypertensive heart disease	336	2,485	212	1,742	97	1,043
Hypertensive renal disease	14	290	5	190	1	119
Hypertensive renal and heart disease	21	217	13	136	8	72
Secondary hypertension	8	43	3	27	1	12

(Table continues next page)

[a] NEC = not elsewhere classified.

Table F.6 (*continued*). Number of Subjects Having at Least One Diagnosis Used to Define Respiratory, Cardiovascular, and Cancer Indices

Diagnosis	1 Year Prior to Death		6 Months Prior to Death		2 Months Prior to Death	
	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects
Congestive Heart Failure						
Heart failure (includes: congestive, left heart, unspecified)	1,252	20,755	748	17,343	343	13,158
Acute Coronary Artery Disease						
Acute myocardial infarction	413	11,420	222	10,065	85	8,576
Other acute and subacute forms of ischemic heart disease	407	4,086	229	3,016	108	1,979
Chronic Coronary Artery Disease						
Old myocardial infarction	535	3,336	355	2,324	166	1,345
Angina pectoris	1,973	12,828	1,230	9,558	554	5,979
Other forms of chronic ischemic heart disease	2,532	16,581	1,749	12,627	790	8,064
Cerebrovascular Disease						
Subarachnoid hemorrhage	7	444	4	419	4	385
Intracerebral hemorrhage	26	1,281	14	1,202	6	1,103
Other and unspecified intracranial hemorrhage	26	702	17	590	6	478
Occlusion and stenosis of precerebral arteries	152	905	89	652	39	389
Occlusion of cerebral arteries	195	3,811	123	3,133	43	2,367
Transient cerebral ischemia	306	1,631	171	1,058	62	548
Acute, but ill-defined, cerebrovascular disease	535	9,252	324	7,804	140	6,106
Other and ill-defined cerebrovascular disease	503	5,500	284	4,272	130	2,955
Late effects of cerebrovascular disease	36	327	27	246	15	164
Chest Pain	1,839	10,518	1017	7,473	380	4,330
Chronic Rheumatic Heart Disease						
Chronic rheumatic pericarditis	1	14	0	10	0	4
Diseases of the mitral valve	200	1,909	124	1,449	63	927
Diseases of the aortic valve	151	1,278	101	968	43	572
Diseases of mitral and aortic valves	29	472	19	357	10	193

(Table continues next page)

[a] NEC = not elsewhere classified.

Table F.6 (*continued*). Number of Subjects Having at Least One Diagnosis Used to Define Respiratory, Cardiovascular, and Cancer Indices

Diagnosis	1 Year Prior to Death		6 Months Prior to Death		2 Months Prior to Death	
	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects
Cancer (Malignant Neoplasms)						
Eye	10	161	6	127	4	82
Lip	3	52	3	39	1	18
Tongue	11	369	8	300	3	182
Major salivary glands	9	116	6	84	3	57
Gum	2	46	1	33	0	20
Floor of mouth	4	161	2	122	2	67
Other and unspecified parts of mouth	17	360	10	264	5	148
Oropharynx	10	293	7	220	3	114
Nasopharynx	3	167	2	129	0	69
Hypopharynx	3	168	1	124	0	72
Ill-defined and other sites within the lip, oral cavity, and pharynx	4	444	3	354	1	219
Ill-defined and other sites within the digestive organs and peritoneum	6	416	3	338	2	243
Esophagus	12	847	8	759	5	563
Stomach	22	2,017	13	1,802	4	1,337
Small intestine and duodenum	2	141	1	108	0	69
Colon	178	4,219	122	3,589	63	2,595
Rectum, rectosigmoid junction, and anus	85	2,346	57	1,897	28	1,211
Liver and intrahepatic bile ducts	6	1,118	3	1,001	0	779
Gallbladder and extrahepatic bile ducts	5	379	5	332	3	251
Pancreas	6	1,554	3	1,442	2	1,144
Retroperitoneum and peritoneum	0	168	0	133	0	94
Nasal cavities, middle ear, and accessory sinuses	5	166	4	127	4	71
Larynx	29	973	21	768	11	448
Trachea, bronchus, and lung	127	12,123	97	11,136	53	9,161
Pleura	0	128	0	100	0	53
Thymus, heart, and mediastinum	3	67	2	51	1	31
Ill-defined and other sites within the respiratory system and intrathoracic organs	1	95	1	82	1	57
Bone and articular cartilage	14	573	5	458	3	278
Connective and other soft tissue	23	500	19	406	5	259
Malignant melanoma of skin	62	480	38	369	13	239
Other skin	372	1,648	231	1,143	86	606
Female breast	344	4,615	263	3,981	139	2,943
Male breast	2	30	0	22	0	9

(Table continues next page)

[a] NEC = not elsewhere classified.

Table F.6 (*continued*). Number of Subjects Having at Least One Diagnosis Used to Define Respiratory, Cardiovascular, and Cancer Indices

Diagnosis	1 Year Prior to Death		6 Months Prior to Death		2 Months Prior to Death	
	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects
Cancer (Malignant Neoplasms) *(continued)*						
Uterus, part unspecified	10	237	6	176	2	111
Cervix uteri	18	709	13	552	7	341
Placenta	2	42	0	30	0	17
Body of uterus	29	573	19	421	8	265
Ovary and other uterine adnexa	18	1,056	15	912	7	655
Other and unspecified female genital organs	9	201	6	144	0	83
Prostate	369	2,786	286	2,339	162	1,645
Testis	11	127	5	100	1	60
Penis and other male genital organs	1	68	1	52	1	20
Bladder	207	1,708	159	1,420	82	914
Kidney and other and unspecified urinary organs	45	986	27	833	10	565
Brain	20	1,956	13	1,670	9	1,172
Other and unspecified parts of nervous system	2	427	2	369	1	237
Thyroid gland	16	170	13	141	10	92
Other endocrine glands and related structures	4	112	1	88	0	58
Ill-defined and other sites	33	762	23	595	10	345
Malignant neoplasm without specification of site	176	13,435	103	11,993	55	9,167
Secondary and unspecified malignant neoplasm of lymph nodes	10	1,098	6	895	3	618
Secondary malignant neoplasm of respiratory and digestive systems	41	2,004	26	1,700	12	1,193
Secondary malignant neoplasm of other specified sites	8	1,287	6	1,037	5	663
Kaposi sarcoma	1	28	0	16	0	8
Lymphosarcoma and reticulosarcoma	19	616	14	537	6	414
Hodgkin disease	16	471	11	393	4	277
Lymphoid and histiocytic neoplasms, other	62	2,069	49	1,803	24	1,393
Multiple myeloma and immunoproliferative neoplasms	29	852	23	755	14	606
Lymphoid leukemia	48	868	34	751	19	581
Myeloid leukemia	7	695	5	612	3	501
Monocytic leukemia	2	41	2	31	0	24
Other specified leukemia	3	137	3	103	1	70
Leukemia of unspecified cell type	23	1,280	19	1,145	7	920

(Table continues next page)

[a] NEC = not elsewhere classified.

Table F.6 *(continued).* Number of Subjects Having at Least One Diagnosis Used to Define Respiratory, Cardiovascular, and Cancer Indices

Diagnosis	1 Year Prior to Death		6 Months Prior to Death		2 Months Prior to Death	
	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects	Comparison Population	Deceased Subjects
Cancer (Malignant Neoplasms) *(continued)*						
Neoplasm of uncertain behavior of digestive and respiratory systems	68	654	34	448	12	217
Neoplasm of uncertain behavior of genitourinary organs	15	183	4	133	1	78
Neoplasm of uncertain behavior of endocrine glands and nervous system	6	101	1	82	1	45
Neoplasm of uncertain behavior of other and unspecified sites and tissues	66	650	39	497	20	320
Neoplasms of unspecified nature	255	8,359	160	6,801	56	4,755

[a] NEC = not elsewhere classified.

Table F.7. Agreement Between Indicators of Disease Group and Hospital Discharge Diagnoses for 39,304 Deceased Subjects Hospitalized Within 2 Months Before Death, 1991 to 1993

Morbidity Index Defined During 2 Months Prior to Death	Total Deaths	% Perfect Agreement (p_0)	95% CI for p_0 (%)	κ	95% CI for κ
Congestive heart failure	4,457	83.5	83.2–83.9	0.38	0.37–0.39
Acute coronary artery disease	3,847	90.1	89.8–90.4	0.50	0.49–0.52
Cerebrovascular disease	4,370	88.8	88.5–89.0	0.52	0.51–0.54
Hypertension	813	84.0	83.6–84.3	0.07	0.06–0.08
Chronic coronary artery disease	4,333	79.7	79.4–80.1	0.25	0.24–0.26
Chronic rheumatic heart disease	744	97.7	97.5–97.8	0.24	0.21–0.27
Acute lower respiratory disease	6,885	76.5	76.1–76.9	0.26	0.25–0.27
Chronic upper respiratory disease	295	98.8	98.7–98.9	0.11	0.08–0.15
Acute upper respiratory disease	615	98.1	98.0–98.2	0.02	0.00–0.03
Airways disease	6,696	78.0	77.6–78.4	0.32	0.31–0.33
Cancer	14,155	87.2	86.9–87.5	0.73	0.72–0.74

Table F.8. Agreement Between Indicators of Disease Group and Hospital Discharge Diagnoses for 41,717 Deceased Subjects Hospitalized Within 6 Months Before Death, 1991 to 1993

Morbidity Index Defined During 6 Months Prior to Death	Total Deaths	% Perfect Agreement (p_0)	95% CI for p_0 (%)	κ	95% CI for κ
Congestive heart failure	6,026	83.5	83.2–83.8	0.42	0.41–0.43
Acute coronary artery disease	4,791	89.2	88.9–89.5	0.48	0.47–0.50
Cerebrovascular disease	5,743	87.9	87.6–88.2	0.52	0.51–0.53
Hypertension	1,871	83.6	83.2–83.9	0.12	0.11–0.14
Chronic coronary artery disease	6,713	79.1	78.8–79.5	0.30	0.29–0.32
Chronic rheumatic heart disease	1,170	96.9	96.8–97.1	0.22	0.19–0.25
Acute lower respiratory disease	9,511	74.0	73.6–74.4	0.25	0.23–0.26
Chronic upper respiratory disease	698	97.9	97.8–98.0	0.09	0.07–0.12
Acute upper respiratory disease	1,402	96.3	96.2–96.5	0.01	0.00–0.02
Airways disease	9,667	76.3	75.9–76.7	0.33	0.32–0.34
Cancer	16,770	88.5	88.2–88.8	0.76	0.76–0.77

Table F.9. Agreement Between Indicators of Disease Group and Hospital Discharge Diagnoses for 43,557 Deceased Subjects Hospitalized Within 1 Year Before Death, 1991 to 1993

Morbidity Index Defined During 1 Year Prior to Death	Total Deaths	% Perfect Agreement (p_0)	95% CI for p_0 (%)	κ	95% CI for κ
Congestive heart failure	7,343	83.2	82.8–83.5	0.43	0.42–0.44
Acute coronary artery disease	5,658	88.3	88.0–88.6	0.46	0.45–0.47
Cerebrovascular disease	6,981	86.8	86.5–87.2	0.50	0.49–0.52
Hypertension	3,420	82.7	82.4–83.1	0.18	0.17–0.19
Chronic coronary artery disease	8,731	78.2	77.8–78.5	0.32	0.31–0.33
Chronic rheumatic heart disease	1,545	96.3	96.1–96.5	0.21	0.18–0.23
Acute lower respiratory disease	11,818	71.4	71.0–71.8	0.22	0.21–0.23
Chronic upper respiratory disease	1,232	96.8	96.6–96.9	0.07	0.05–0.09
Acute upper respiratory disease	2,455	94.1	93.9–94.3	0.01	0.00–0.01
Airways disease	12,122	74.4	74.1–74.8	0.32	0.31–0.33
Cancer	18,258	88.0	87.7–88.3	0.75	0.75–0.76

Table F.10. Distribution of Selected Variables for the Two Study Groups

	Deceased Subjects		Comparison Population	
	Number	Percent	Number	Percent
Sex				
Men	72,752	51.6	25,896	52.2
Women	68,187	48.4	23,666	47.8
Age (Years)				
≤ 1	275	0.2	169	0.3
2–9	296	0.2	188	0.4
10–19	570	0.4	304	0.6
20–34	3,586	2.5	1,462	2.9
35–64	31,632	22.4	12,025	24.3
65–74	34,531	24.5	12,100	24.4
≥ 75	70,049	49.7	23,314	47.0
Reference Year[a]				
1984	13,289	9.4	N/A	N/A
1985	13,684	9.7	N/A	N/A
1986	13,761	9.8	N/A	N/A
1987	14,154	10.0	6,963	14.0
1988	13,928	9.9	6,940	14.0
1989	14,371	10.2	7,079	14.3
1990	13,933	9.9	6,874	13.9
1991	14,490	10.3	7,127	14.4
1992	14,248	10.1	7,089	14.3
1993	15,081	10.7	7,490	15.1
Total	140,939		49,562	

[a] Year in which comparison subjects were selected or deceased subjects died. N/A = not applicable.

Table F.11. Logistic Regression Results for Each Morbidity Index Adjusted for Age, Sex, and All Other Indices Listed, Excluding Accidental Deaths, According to Time Interval Prior to Reference Date[a]

	1 Year Before Reference Date[b]		6 Months Before Reference Date		2 Months Before Reference Date	
Index of Disease Group	Odds Ratio	95% CI	Odds Ratio	95%CI	Odds Ratio	95% CI
Congestive heart failure	4.21	3.93–4.53	5.78	5.27–6.35	8.71	7.58–10.06
Hypertension	0.54	0.51–0.57	0.53	0.50–0.57	0.72	0.64–0.82
Chronic rheumatic heart disease	1.55	1.38–1.76	1.74	1.50–2.03	1.81	1.48–2.24
Acute coronary artery disease	5.97	5.53–6.46	8.67	7.85–9.59	13.03	11.29–15.14
Chronic coronary artery disease	1.30	1.24–1.36	1.41	1.34–1.48	1.73	1.61–1.86
Cerebrovascular disease	4.21	3.97–4.47	5.65	5.26–6.08	8.14	7.35–9.05
Acute lower respiratory disease	2.66	2.55–2.78	3.96	3.74–4.21	5.10	4.70–5.54
Chronic upper respiratory disease	0.57	0.52–0.62	0.55	0.49–0.62	0.50	0.41–0.60
Acute upper respiratory disease	0.52	0.49–0.55	0.51	0.48–0.56	0.43	0.39–0.48
Airways disease	1.59	1.54–1.65	1.73	1.66–1.80	1.74	1.66–1.83
Cancer	9.58	9.19–10.00	11.37	10.84–11.94	13.65	12.82–14.55
No billings	1.96	1.89–2.04	2.31	2.24–2.39	3.50	3.41–3.60
Arrhythmia	1.30	1.22–1.38	1.49	1.38–1.61	1.92	1.71–2.17
Atherosclerosis	1.73	1.61–1.86	1.96	1.80–2.13	2.36	2.10–2.67
Diabetes	1.68	1.60–1.77	1.66	1.57–1.76	1.68	1.56–1.81
Dementia	1.07	0.96–1.20	0.98	0.85–1.12	0.96	0.81–1.14
Peripheral vascular disease	1.92	1.73–2.13	2.31	2.04–2.62	3.41	2.84–4.13
Ulcer disease	1.57	1.42–1.73	1.75	1.55–2.00	2.20	1.83–2.68
Connective tissue	0.81	0.71–0.93	0.82	0.70–0.97	0.78	0.62–0.97
Neurological conditions	3.19	2.96–3.44	3.71	3.39–4.08	3.77	3.34–4.26
Renal disease	3.84	3.53–4.19	4.92	4.43–5.48	7.05	6.08–8.22

[a] Includes nonaccidental deaths only.

[b] The time interval is measured backwards from the reference date. The reference date is defined for a control subject as the date of the last medical interaction in the year in which the control subject was selected or the last day of that year if there were no billings in that year. The reference date for a deceased subject is the date of death.

COMPARISON OF MORBIDITY INDICES TO CAUSES OF DEATH

Table F.13 presents the comparisons of morbidity indices to underlying causes of death as recorded on death certificates. The columns in the tables present the percentage of subjects attributed to each disease group from QHIP data according to the coded underlying cause of death. We found excellent agreement between the morbidity indices and underlying cause of death for cancer and moderate agreement for cardiovascular diseases. For subjects classified as having only respiratory diseases, the underlying cause of death was attributed almost equally to circulatory and respiratory diseases. For subjects with comorbid conditions that included cancer, the underlying cause of death was more likely to be attributed to cancer than to other comorbid conditions.

Table F.12. Diagnoses Used in Definition of Other Conditions Considered in Case-Control Analyses

ICD-9 Code	Description
Arrhythmia	
306	Physiological malfunction arising from mental factors
426	Conduction disorders
427	Cardiac dysrhythmias
780	General symptoms
997	Complications affecting specified body systems, not elsewhere classified
Atherosclerosis	
440	Atherosclerosis
Connective tissue	
710	Diffuse diseases of connective tissue
714	Rheumatoid arthritis and other inflammatory polyarthropathies
725	Polymyalgia rheumatica
Dementia	
290	Senile and presenile organic psychotic conditions
Diabetes	
250	Diabetes mellitus
Dysrhythmia	
427	Cardiac dysrhythmias
Liver disease	
456	Varicose veins of other sites
571	Chronic liver disease and cirrhosis
572	Liver abscess and sequelae of chronic liver disease
Peripheral vascular disease	
441	Aortic aneurysm and dissection
443	Other peripheral vascular disease
785	Symptoms involving cardiovascular system
V43	Organ or tissue replaced by other means
Neurological conditions	
013	Tuberculosis of meninges and central nervous system
036	Meningococcal infection
046	Slow virus infection of central nervous system
269	Other nutritional deficiencies
290	Senile and presenile organic psychotic conditions
294	Other organic psychotic conditions (chronic)
310	Specific nonpsychotic mental disorders due to organic brain damage
320	Bacterial meningitis

(Table continues next column)

Table F.12 *(continued).* Diagnoses Used in Definition of Other Conditions Considered in Case-Control Analyses

ICD-9 Code	Description
Neurological conditions *(continued)*	
321	Meningitis due to other organisms
322	Meningitis of unspecified cause
323	Encephalitis, myelitis, and encephalomyelitis
324	Intracranial and intraspinal abscess
325	Phlebitis and thrombophlebitis of intracranial venous sinuses
326	Late effects of intracranial abscess or pyogenic infection
330	Cerebral degenerations usually manifest in childhood
331	Other cerebral degenerations
332	Parkinson's disease
333	Other extrapyramidal disease and abnormal movement disorders
334	Spinocerebellar disease
335	Anterior horn cell disease
336	Other diseases of spinal cord
337	Disorders of the autonomic nervous system
342	Hemiplegia and hemiparesis
348	Other conditions of brain
349	Other and unspecified disorders of the nervous system
352	Disorders of other cranial nerves
742	Other congenital anomalies of nervous system
Renal disease	
580	Acute glomerulonephritis
581	Nephrotic syndrome
582	Chronic glomerulonephritis
583	Nephritis and nephropathy, not specified as acute or chronic
584	Acute renal failure
585	Chronic renal failure
586	Renal failure, unspecified
587	Renal sclerosis, unspecified
588	Disorders resulting from impaired renal function
589	Small kidney of unknown cause
590	Infections of kidney
591	Hydronephrosis
592	Calculus of kidney and ureter
593	Other disorders of kidney and ureter
Ulcer disease	
531	Gastric ulcer
532	Duodenal ulcer
533	Peptic ulcer, site unspecified
534	Gastrojejunal ulcer

Table F.13. Causes of Death According to Each Disease Group, Montreal, 1984 to 1993[a]

Cause of Death	No Billings	No Index Defined	Cancer Only	Respiratory Only	Cardiovascular Only	Cancer & Respiratory	Cancer & Cardiovascular	Respiratory & Cardiovascular	Cancer, Respiratory, & Cardiovascular
1 Year Prior to Death (*n* Values)	**5,204**	**29,257**	**16,565**	**15,613**	**20,992**	**14,668**	**5,260**	**19,131**	**7,214**
Infectious & parasitic diseases	0.98	1.74	0.91	5.91	0.67	2.80	0.49	1.29	0.83
Neoplasms	15.30	11.70	88.65	9.19	3.62	84.05	67.02	3.12	63.64
Endocrine, nutritional, metabolic diseases; immunity disorders	3.61	5.76	0.69	4.20	5.22	0.65	1.63	4.57	1.22
Diabetes	2.36	4.31	0.45	2.50	4.33	0.29	1.29	3.91	0.85
Diseases of blood & blood-forming organs	0.31	0.71	0.21	0.61	0.36	0.27	0.40	0.36	0.36
Mental disorders	3.77	3.41	0.24	1.95	0.96	0.18	0.32	0.70	0.24
Diseases of nervous system & sense organs	3.75	5.69	0.41	4.57	1.79	0.50	0.53	1.46	0.53
Diseases of circulatory system	55.61	50.45	5.14	36.31	77.94	4.77	24.35	68.52	23.15
Diseases of respiratory system	8.24	7.70	1.36	26.52	3.16	4.81	1.96	12.52	6.65
Diseases of digestive system	3.34	8.11	1.73	6.74	3.61	1.40	2.09	3.71	1.86
Diseases of genitourinary system	1.19	2.29	0.43	1.97	1.91	0.30	0.89	2.84	1.07
Symptoms, signs, & ill-defined conditions	2.94	1.27	0.10	0.72	0.34	0.07	0.13	0.22	0.11
6 Months Prior to Death (*n* Values)	**6,999**	**34,809**	**19,599**	**15,682**	**20,949**	**12,423**	**4,195**	**14,903**	**4,345**
Infectious & parasitic diseases	0.83	2.05	0.92	5.58	0.64	2.46	0.45	1.28	0.87
Neoplasms	14.57	13.26	90.20	9.99	3.50	84.51	67.06	3.02	63.64
Endocrine, nutritional, metabolic diseases; immunity disorders	3.73	5.67	0.57	4.03	5.06	0.58	1.41	4.44	1.15
Diabetes	2.54	4.29	0.34	2.35	4.28	0.27	1.19	3.75	0.71
Diseases of blood & blood-forming organs	0.29	0.69	0.20	0.60	0.35	0.25	0.50	0.33	0.35
Mental disorders	3.81	3.08	0.16	1.70	0.79	0.15	0.31	0.58	0.25
Diseases of nervous system & sense organs	4.21	5.17	0.29	4.17	1.55	0.46	0.60	1.37	0.46
Diseases of circulatory system	56.01	50.17	4.46	35.92	79.06	4.67	24.08	68.66	23.48
Diseases of respiratory system	8.43	7.45	1.22	27.88	3.13	5.08	2.29	13.03	6.35
Diseases of digestive system	3.11	7.88	1.48	6.38	3.28	1.30	2.03	3.60	1.80
Diseases of genitourinary system	1.21	2.34	0.32	2.01	1.93	0.26	0.95	2.82	1.15
Symptoms, signs, & ill-defined conditions	2.89	1.10	0.09	0.57	0.28	0.05	0.17	0.19	0.14

(Table continues next page)

[a] All data expressed as percentage of total.

Table F.13 *(continued).* Major Causes of Death According to Each Disease Group, Montreal, 1984 to 1993[a]

Major Cause of Death	No Billings	No Index Defined	Cancer Only	Respiratory Only	Cardiovascular Only	Cancer & Respiratory	Cancer & Cardiovascular	Respiratory & Cardiovascular	Cancer, Respiratory, & Cardiovascular
2 Months Prior to Death (*n* Values)	**11,491**	**42,993**	**21,527**	**15,188**	**19,866**	**8,416**	**2,549**	**10,044**	**1,830**
Infectious & parasitic diseases	0.75	2.44	0.86	5.06	0.63	2.08	0.55	1.00	0.71
Neoplasms	18.29	17.85	91.57	11.41	3.38	84.17	66.10	3.20	63.22
Endocrine, nutritional, metabolic diseases; immunity disorders	4.06	5.46	0.43	3.73	4.62	0.53	1.06	3.96	1.20
Diabetes	3.02	4.08	0.24	2.31	3.94	0.26	0.86	3.32	0.71
Diseases of blood & blood-forming organs	0.26	0.66	0.20	0.57	0.34	0.25	0.63	0.29	0.33
Mental disorders	3.32	2.60	0.14	1.35	0.63	0.12	0.16	0.58	0.16
Diseases of nervous system & sense organs	3.97	4.48	0.22	3.71	1.36	0.38	0.51	1.18	0.49
Diseases of circulatory system	54.36	47.58	3.75	35.32	80.46	4.80	25.30	69.21	23.93
Diseases of respiratory system	7.75	7.18	1.15	29.71	3.13	5.62	2.43	13.72	6.78
Diseases of digestive system	2.92	7.44	1.27	5.72	2.93	1.38	2.12	3.44	1.48
Diseases of genitourinary system	1.04	2.38	0.26	1.95	1.92	0.32	0.75	2.71	1.31
Symptoms, signs, & ill-defined conditions	2.52	0.87	0.05	0.42	0.17	0.08	0.24	0.10	0.05

[a] All data expressed as percentage of total.

Table F.14. Joint Distribution of the Attribution of Deceased Subjects to Specific Groups by Time Period Before Death, Montreal, 1984 to 1993[a]

Time Period Prior to Death (in months)			> 65 Years		≥ 65 Years		> 65 Years		≥ 65 Years	
0–2	≥ 2–6	≥ 6–12	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
			Congestive Heart Failure				**Hypertension**			
Y	N	N	844	2.3	5,445	5.2	203	0.6	1,020	1.0
N	Y	N	305	0.8	2,063	2.0	179	0.5	1,046	1.0
N	N	Y	327	0.9	2,451	2.3	380	1.0	2,326	2.2
Y	Y	N	244	0.7	1,336	1.3	30	0.1	155	0.1
Y	N	Y	105	0.3	759	0.7	22	0.1	141	0.1
N	Y	Y	136	0.4	817	0.8	76	0.2	676	0.6
Y	Y	Y	158	0.4	1,009	1.0	21	0.1	217	0.2
N	N	N	29,637	81.5	88,268	84.4	30,845	84.8	96,567	92.3
			Acute Coronary Artery Disease				**Chronic Coronary Artery Disease**			
Y	N	N	1,537	4.2	6,846	6.5	1,041	2.9	4,778	4.6
N	Y	N	299	0.8	1,389	1.3	604	1.7	2,790	2.7
N	N	Y	386	1.1	1,652	1.6	816	2.2	3,907	3.7
Y	Y	N	115	0.3	645	0.6	275	0.8	1,204	1.2
Y	N	Y	94	0.3	341	0.3	244	0.7	1,127	1.1
N	Y	Y	87	0.2	369	0.4	464	1.3	1,941	1.9
Y	Y	Y	53	0.1	269	0.3	503	1.4	1,912	1.8
N	N	N	29,185	80.3	90,637	86.7	27,809	76.5	84,489	80.8
			Cerebrovascular Disease				**Chronic Rhumatic Heart Disease**			
Y	N	N	1,389	3.8	6,203	6.0	169	0.5	673	0.3
N	Y	N	376	1.0	1,923	1.8	117	0.3	494	0.5
N	N	Y	389	1.1	2,395	2.3	131	0.4	581	0.6
Y	Y	N	147	0.4	1,201	1.1	40	0.1	123	0.1
Y	N	Y	59	0.2	495	0.5	23	0.1	103	0.1
N	Y	Y	133	0.4	738	0.7	67	0.2	190	0.2
Y	Y	Y	109	0.3	1,159	1.1	126	0.4	216	0.2
N	N	N	29,154	80.2	87,935	84.1	31,080	85.5	99,768	95.4
			Acute Upper Respiratory Disease				**Chronic Upper Respiratory Disease**			
Y	N	N	329	0.9	873	0.8	179	0.5	328	0.3
N	Y	N	488	1.3	1,012	1.3	240	0.7	468	0.4
N	N	Y	797	2.2	1,537	1.5	379	1.0	703	0.7
Y	Y	N	39	0.1	57	0.1	19	0.1	39	0.0
Y	N	Y	28	0.1	60	0.1	11	0.0	23	0.0
N	Y	Y	100	0.3	126	0.1	40	0.1	79	0.1
Y	Y	Y	22	0.1	24	0.0	11	0.0	22	0.0
N	N	N	29,953	82.4	98,459	94.1	30,877	84.9	100,486	96.1

(Table continues next page)

[a] Includes nonaccidental deaths only.

Table F.14, *(continued).* Joint Distribution of the Attribution of Deceased Subjects to Specific Groups by Time Period Before Death, Montreal, 1984 to 1993[a]

Time Period Prior to Death (in months)			> 65 Years		≥ 65 Years		> 65 Years		≥ 65 Years	
0–2	≥ 2–6	≥ 6–12	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
			Acute Lower Respiratory Disease				**Airways Disease**			
Y	N	N	2,282	6.3	9,847	9.4	922	2.5	4,147	4.0
N	Y	N	1,118	3.1	3,337	3.2	588	1.6	2,556	2.4
N	N	Y	1,308	3.6	3,800	3.6	726	2.0	4,089	3.9
Y	Y	N	393	1.1	1,379	1.3	224	0.6	2,225	2.1
Y	N	Y	288	0.8	907	0.9	120	0.3	912	0.9
N	Y	Y	327	0.9	711	0.7	234	0.6	2,225	2.1
Y	Y	Y	219	0.6	460	0.4	321	0.9	8,702	8.3
N	N	N	25,821	71.0	81,707	78.1	28,621	78.7	76,402	73.1
			Cancer							
Y	N	N	2,864	7.9	8,367	8.0				
N	Y	N	721	2.0	2,282	2.2				
N	N	Y	681	1.9	2,459	2.4				
Y	Y	N	2,649	7.3	4,440	4.2				
Y	N	Y	516	1.4	1,343	1.3				
N	Y	Y	971	2.7	2,282	2.2				
Y	Y	Y	6,062	16.7	8,131	7.8				
N	N	N	17,292	47.6	72,844	69.7				

[a] Includes nonaccidental deaths only.

Table F.15. Synthesis of Results of the Mean Percent Change for the Different Disease Groups for Selected Measures of Particulates Evaluated at the Interquartile Range, Montreal, 1984 to 1993[a]

Group	COH	Extinction	TSP	PM_{10}	$PM_{2.5}$	Predicted $PM_{2.5}$	Sulfate from Sutton	Sulfate from $PM_{2.5}$	Predicted Sulfate from $PM_{2.5}$
Lag 0 Days									
No Billings	2.89	1.19	−1.93	−3.02	−7.38[b]	4.68[b]	2.17	−2.31	2.76[b]
Cancer	1.27[b]	1.48[b]	1.43	2.67	2.19	1.72[b]	1.08[b]	3.72[b]	1.51[b]
Respiratory Disease									
Acute upper respiratory disease	1.66	−1.58	24.22[b]	N/C	N/C	4.08	3.30	N/C	3.64
Chronic upper respiratory disease	−0.33	−4.15	5.94	11.51[b]	7.24	−0.08	0.56	N/C	−0.08
Acute lower respiratory disease	1.04	1.42	3.81	1.42	1.26	2.12[b]	1.09	−0.13	1.52
Airways disease	0.61	1.24	−0.40	−0.89	−1.28	1.47[b]	0.14	−1.39	0.90
Cardiovascular Disease									
Acute coronary artery disease	1.51	1.06	7.43[b]	2.94	1.73	1.94	0.43	−0.61	0.95
Chronic coronary artery disease	1.76[b]	1.11	2.14	0.41	2.33	1.66	0.41	2.95	0.85
Congestive heart failure	2.88[b]	2.98[b]	5.45[b]	0.90	2.13	3.44[b]	1.67[b]	0.09	2.61[b]
Hypertension	1.65	1.53	0.12	−2.07	0.60	1.97	0.23	N/C	1.12
Cerebrovascular disease	0.69	0.53	−1.19	1.23	1.36	1.72	0.42	−1.48	0.88
Any coronary artery disease	1.40	0.66	3.76	1.59	1.66	1.74[b]	0.73	2.19	1.02
Any cardiovascular disease	1.82[b]	1.10[b]	1.30	0.86	1.19	2.05[b]	0.72	0.78	1.19[b]
Lag 1 Day									
No Billings	−0.68	2.78	9.20	N/C	−0.81	2.94	1.61	N/C	2.51
Cancer	1.39[b]	0.79	0.74	−0.79	0.66	1.31[b]	0.54	0.89	0.81
Respiratory Disease									
Acute upper respiratory disease	3.72	0.68	3.17	N/C	N/C	5.14	3.73	N/C	4.11
Chronic upper respiratory disease	2.92	−2.32	2.77	0.04	N/C	1.39	1.64	N/C	0.63
Acute lower respiratory disease	4.38[b]	0.59	4.91	3.74	3.53	3.27[b]	1.83[b]	4.61[b]	1.86[b]
Airways disease	1.44	1.41[b]	6.60[b]	2.29	N/C	1.11	0.60	2.65	0.95
Cardiovascular Disease									
Acute coronary artery disease	2.31	0.70	−5.14	−0.33	0.48	2.38	0.68	−0.29	1.09
Chronic coronary artery disease	1.98[b]	0.25	4.09	3.50	3.08	1.82[b]	0.66	1.42	0.98
Congestive heart failure	4.17[b]	1.58	0.94	3.78	4.08	2.81[b]	1.18	2.91	1.53[b]
Hypertension	1.99	0.57	−0.76	2.70	2.54	0.34	0.14	N/C	0.23
Cerebrovascular disease	1.71	0.96	8.09[b]	3.85	1.70	1.77	1.03	1.23	1.13
Any coronary artery disease	2.56[b]	0.35	2.37	1.90	2.00	1.60[b]	0.30	0.97	0.61
Any cardiovascular disease	2.95[b]	1.14[b]	2.75	2.70[b]	2.51[b]	2.49[b]	1.11[b]	2.31[b]	1.52[b]

(Table continues next page)

[a] The statistical model was $E[\log(y_i)] = \alpha$ + LOESS(i, span=91/3,653) + LOESS(year) + LOESS(Mean temperature$_0$, Change in barometric pressure from the previous 24 hours$_0$) + $\beta \times$ (pollutant), where y_i is the number of nonaccidental deaths on day i for subjects included in each group. N/C = convergence of model not attained.

[b] Corrected t value > 1.96.

Table F.15 (*continued*). Synthesis of Results of the Mean Percent Change for the Different Disease Groups for Selected Measures of Particulates Evaluated at the Interquartile Range, Montreal, 1984 to 1993[a]

Group	COH	Extinction	TSP	PM_{10}	$PM_{2.5}$	Predicted $PM_{2.5}$	Sulfate from Sutton	Sulfate from Sutton	Predicted Sulfate from $PM_{2.5}$
3-Day Mean									
No Billings	0.84	1.82				4.70[b]	3.18[b]		3.30[b]
Cancer	2.42[b]	1.52[b]				1.84[b]	0.89		1.14[b]
Respiratory Disease									
Acute upper respiratory disease	4.57	–0.95				7.28	6.36[b]		6.56[b]
Chronic upper respiratory disease	2.39	–2.38				3.81	4.34[b]		3.41
Acute lower respiratory disease	5.09[b]	1.71				4.72[b]	2.25[b]		2.90[b]
Airways disease	1.53	2.08[b]				1.33	0.51		1.02
Cardiovascular Disease									
Acute coronary artery disease	2.35	1.30				2.27	0.99		1.30
Chronic coronary artery disease	2.62[b]	1.59				2.20[b]	0.63		1.28
Congestive heart failure	4.99[b]	3.24[b]				4.02[b]	1.91[b]		2.64[b]
Hypertension	3.35	1.36				1.88	0.53		0.87
Cerebrovascular disease	1.73	0.32				1.53	0.63		0.70
Any coronary artery disease	2.99[b]	1.10				1.85[b]	0.69		0.98
Any cardiovascular disease	3.65[b]	1.65[b]				2.76[b]	1.16[b]		1.53[b]

[a] The statistical model was $E[\log(y_i)] = \alpha$ + LOESS(i, span=91/3,653) + LOESS(year) + LOESS(Mean temperature$_0$, Change in barometric pressure from the previous 24 hours$_0$) + $\beta \times$ (pollutant), where y_i is the number of nonaccidental deaths on day i for subjects included in each group. N/C = convergence of model not attained.

[b] Corrected t value > 1.96.

APPENDIX G. HEI Quality Assurance Report

The conduct of this study was subjected to periodic, independent audits by a team from Hoover Consultants. This team consisted of an auditor with experience in toxicology and epidemiology and a physician with epidemiology experience. The audits included in-process monitoring of study activities for conformance to the study protocol and examination of records and supporting data. The dates of each audit are listed below with the phase of the study examined.

Quality Assurance Audits

Date	Phase of Study Audited
March 25–26, 1997	All records for a sample of randomly chosen cases were audited for the interval of one year prior to death. The auditors compared the disease designation used in the study to the documentation supporting the designation. The prescription database was used to identify medications used for three broad categories of disease: respiratory, cardiovascular, and cancer. The auditors tracked documentation of the methods used to assign the drug identification number and screen the database for a medication chosen at random. The auditors tracked the methods used to group generic drugs with multiple brands (each brand with a drug identification number). Procedures for obtaining and using air pollution data were audited for consistency with program documents. Data collection, uploading, and editing of data were audited.
January 18–19, 1999	Previous audit findings were followed up and a random sample of subjects was chosen for audit as described above. The text was scanned, but since it was an early draft, the audit mainly focused on the tables in the draft final report. The auditors compared the reported numbers to the data in hard copy files and, in cases of discrepancies, reported data were compared with the data in the computer system. If errors were noted, the database was queried and the values recalculated. Due to the complexity of the relative risk estimates, the auditors sat with the statistician while she recalculated some of the numbers based on selected interquartile range data for specific pollutants.

Written reports of each inspection were provided to the Director of Research of the Health Effects Institute who transmitted these findings to the Principal Investigator. These quality assurance audits demonstrated that the study was conducted by a well-coordinated, experienced team of professionals according to the study protocol and standard operating procedures. The report appears to be an accurate representation of the study.

B Kristin Hoover, Audit Coordinator
Hoover Consultants

APPENDICES AVAILABLE ON REQUEST

The following appendices may be downloaded as a PDF file from our web site (*www.healtheffects.org*). Hard copies may be requested by contacting the Health Effects Institute at 955 Massachusetts Avenue, Cambridge MA 02139, by phone (617-876-6700), fax (617-876-6709), or e-mail (pubs@healtheffects.org). Please give the full title of the Research Report, the name of the first author, and the titles of the appendices you wish to request.

H. Mean Percent Change in Daily Specified Causes of Death, Evaluated at Lag 0, Lag 1, and 3-Day Mean

I. Plots of Statistical Models

J. Scatterplots of Pollutants Over Time

K. Summary Estimates of Effects of Pollutants on Specific Causes of Death

L. Adequacy of Smoothing and Sensitivity Analyses

M. Results of Analyses: Particulate Effects on Defined Health Conditions

N. Results of Analyses: Particulate Effects on Combined Health Conditions

O. Synthesis of Results for Disease Groups

ABOUT THE AUTHORS

Mark S Goldberg is associate professor at the Institut National de la Recherche Scientifique, University of Quebec, Laval, Quebec, and is adjunct professor at McGill University, Montreal, Quebec. Dr Goldberg obtained degrees in physics (BSc 1975) and epidemiology and biostatistics (MSc 1985; PhD 1992) from McGill University, Montreal, Quebec. Dr Goldberg is currently researching the short-term effects of air pollution on mortality and identification of susceptible groups. He is part of HEI's team to reanalyze the Harvard Six Cities Study and the American Cancer Society's Cancer Prevention Study–II. His other research interests include investigating occupational risk factors for female breast cancer, and delivery of treatment and other health services for breast cancer.

John C Bailar III is professor in the Department of Health Studies and at the Harris School of Public Policy, University of Chicago. He possesses a BA (Colorado, 1953), an MD (Yale, 1955), and a PhD in statistics (American University, 1973). His current research interests include the health effects of particulate air pollution, trends in cancer mortality, food safety, the Gulf War Syndrome, and misconduct in science.

Richard T Burnett is a senior research scientist with the Environmental Health Directorate, Health Canada. Dr Burnett received his BSc in 1977, his MSc in 1978 and his PhD in 1982 from Queen's University, Kingston, Ontario. He is currently investigating the use of administrative health and environmental data to assess the potential risk of environmental contaminants on human health. Dr Burnett is also interested in the use of nonlinear random effects regression models, including survival models.

Jeffrey R Brook is a research scientist in the Air Quality Processes Research Division, Atmospheric Environment Service, Environment Canada, Toronto, and is a lecturer in the Department of Public Health Sciences, University of Toronto. He received his BS from Michigan State University (1982), obtained a diploma in meteorology from McGill University (1983), and received his MS and PhD from the University of Michigan, Ann Arbor, in 1988 and 1991, respectively. Dr Brook's current research interests are in the area of urban air quality, involving atmospheric concentrations, multipollutant human exposures and composition, atmospheric processes and sources of fine particles, and their health effects. Dr Brook also remains actively involved in acidic deposition research on dry deposition as well as fog and cloud water deposition.

Robyn Tamblyn is an associate professor in the Departments of Medicine, Epidemiology, and Biostatistics at McGill University Health Centre and a scientist and codirector of the Centre's Health Services and Outcomes Research. Dr Tamblyn received her BSc (Nursing) in 1973 from McMaster University, Hamilton, Ontario. She completed her MSc in epidemiology in 1982 from McMaster University and her PhD in epidemiology in 1989 from McGill University. Dr Tamblyn's current research interests are medical education, medical practice and patient outcome. She leads the Quebec Research Group on Medication Use in the Elderly while actively participating on several committees both within the university and throughout Canada.

Yvette Bonvalot is a research scientist at the Occupational Health and Environmental Health unit of the Montreal Public Health Department. She is also a research scientist in Toxicological Risk Analysis, University of Montreal. She received her BS in biology from the University of Paris XIII (1984), her MS in environmental engineering from the University of Savoie, France (1986), and her PhD in biomathematics from the University of Paris VII (1993). Dr Bonvalot's current research interests are in public health (quantitative methods in risk assessment), multipollutant human exposure assessment, occupational health (formaldehyde and organophosphate pesticides), and environmental health assessment (urban ambient air, wood combustion products, and climate change).

Pierre Ernst is professor of medicine at McGill University. He is based in the Pharmacoepidemiology unit at Royal Victoria Hospital and his research involves examining the benefits and risk of medications, especially respiratory drugs, among the general population. He is also actively involved in research on the determinants of asthma in children. He receives support from le Fonds de la Recherche en Santé du Québec (FRSQ) and the Medical Research Council of Canada (MRC). His clinical work is carried out principally at the Montreal General Hospital and his primary area of interest is asthma. He has authored or coauthored approximately 100 peer-reviewed publications and has been actively involved in the development of the Canadian asthma treatment guidelines.

Kenneth Flegel is professor of medicine, McGill University, and senior physician and consultant in the Internal Medicine unit at Royal Victoria Hospital, McGill University. His degrees are BSc (McGill University, 1968), MDCM (1972), and MSc (London School of Hygiene and Tropical Medicine, 1986). Dr Flegel conducts clinical research on heart disease and stroke, with special interests in the contribution of atrial fibrillation to the burden and cost of

stroke. His other current areas of research are concept and theory development for medical practice, and diabetes control and complications.

Ravinder K Singh is a biostatistician in the Respiratory Epidemiology unit at McGill University Health Centre. She received her BSc in mathematics (Honors) from Delhi University, India (1977) and an MSc from Delhi University, India (1979). She obtained a second MSc in statistics from Concordia University, Montreal, in 1992. Ms Singh is involved currently in investigations of the impact of microbial contamination in heating, ventilation, and air conditioning systems in office buildings on respiratory and musculoskeletal symptoms in office workers, and in the improvement in health-related quality of life in subjects with chronic obstructive pulmonary disease.

Marie-France Valois is a statistician in the Department of Epidemiology and Biostatistics at McGill University Health Centre. She received her BSc in statistics from Laval University, Ste-Foy, Quebec in 1994 and her MSc in statistics from McGill in 1997. Ms Valois has worked on assessing the performance of the generalized estimating equations method in the analysis of crossover designs and since 1996 has worked exclusively as one of the principal analysts of the current investigation.

OTHER PUBLICATIONS RESULTING FROM THIS RESEARCH

Goldberg MS. 1996. Particulate air pollution and daily mortality. Who is at risk? J Aerosol Med 9:43–53.

ABBREVIATIONS AND OTHER TERMS

AIC	Akaike Information Criterion
CAAMP	Canadian Acid Aerosol Measurement Program
CI	confidence interval
CO	carbon monoxide
CO_2	carbon dioxide
COH	coefficient of haze
df	degrees of freedom
DIN	Drug Identification Number
EPA	US Environmental Protection Agency
GAM	generalized additive model
ICD-9	*International Classification of Diseases, Ninth Revision*
IQR	interquartile range
LOESS	locally weighted smoother
MedEcho	Quebec Hospital Discharge Registry
MPC	mean percent change
MUC	Montreal Urban Community
NAPS	National Air Pollution Surveillance Program of Environment Canada
NO_2	nitrogen dioxide
O_3	ozone
PM	particulate matter
$PM_{2.5}$	particulate matter with an aerodynamic diameter of 2.5 μm or smaller
PM_{10}	particulate matter with an aerodynamic diameter of 10 μm or smaller
QHIP	Quebec Health Insurance Plan
SO_2	sulfur dioxide
SO_4^{2-}	sulfate
TSP	total suspended particles

INTRODUCTION

In 1994, a major objective of HEI's initial research program on particulate matter (PM),* as stated in Request for Applications 94-2, was to fund "*…epidemiologic studies to identify who is at increased risk of mortality from particles and what conditions of pollutant exposure and other factors are associated with increased mortality.*" HEI sought studies that would "*…provide more detailed information about the circumstances surrounding deaths attributed to particulate air pollution.[and].higher resolution data on causes of death than would normally be found on death certificates.*" Dr Goldberg and his colleagues were among those funded from this RFA.†

This study by Goldberg and colleagues takes advantage of the unique opportunities for epidemiologic research offered by the Quebec provincial health insurance system, which allowed the investigators to test hypotheses about whether the health status of populations might increase the risk of mortality associated with air pollution. The records of the Quebec Health Insurance Plan (QHIP) provided a resource for constructing a detailed medical history for each decedent in the Montreal population for the 10-year period of study. This history was linked to mortality records and air pollution monitoring data to examine the role of prior medical history (diagnostic and treatment information, including medication use) in the mortality–air pollution association.

SCIENTIFIC BACKGROUND

Epidemiologic analyses of mid-20th-century air pollution episodes such as the 1952 London Fog indicated that excess mortality was concentrated among people with preexisting cardiovascular, and especially respiratory, diseases (Schwartz 1994; Anderson 1999). More recently, smaller effects have been consistently reported at much lower ambient pollution levels (Pope and Dockery 1999; Samet et al 2000). However, because these studies used routinely collected mortality data obtained from death certificates, few of the studies could describe in detail the clinical conditions of the decedents at the time of, or immediately preceding, their deaths.

Utell and Samet (1993) noted that persons with chronic obstructive pulmonary disease, observed to be at increased risk of mortality in daily time-series studies, have "long been considered susceptible to adverse effects of air pollution." Others hypothesized that those who were dying when air pollution levels increased had chronic cardiovascular or respiratory disease, but may have been relatively well at the time though particularly susceptible for clinically inapparent reasons (Bates 1994). Limited support for this latter view was provided by a study of daily mortality in Philadelphia on days of high PM air pollution (Schwartz 1994). Schwartz observed that among all reported deaths, there was a disproportionate increase in deaths occurring among persons not resident in hospitals or clinics, though others did not observe this increase (Lyon et al 1994).

Also, an important public health question is whether a short-term association between PM and mortality mainly reflects a very small advancement in the time of death (on the order of a few days) among frail individuals. Recent work indicating that deaths are occurring more than a few days after PM levels increase (Zeger et al 1999; Brunekreef and Hoek 2000; Schwartz 2000) and the remaining controversy over this issue might be addressed if data were available on health conditions present before death. Goldberg (1996) noted in a paper that presented the rationale and design of his study: "*…there is considerable interest in whether the short-term effects of air pollution manifest themselves simply by moving forward death dates of persons who would have died a few days later. The identification of sub-groups, especially if accompanied by estimates of survival times, could be used to estimate the public health impact.*" Therefore, this study, in identifying potentially sensitive groups, lays the groundwork for future research to understand how these individuals might be adversely affected by PM.

STUDY AIMS

The investigators of this study had two major objectives: (1) to determine whether concentrations of particles in the

* A list of abbreviations and other terms appears at the end of the Investigators' Report.

† Dr Mark S Goldberg's 3-year study, *Particulate Air Pollution and Daily Mortality in Montreal, Quebec, 1984–1993*, began in July 1995 and had total expenditures of $536,174. The Investigators' Report from Goldberg and colleagues was received for review in June 1999. A revised report, received in December 1999, was accepted for publication in February 2000. During the review process, the HEI Health Review Committee and the investigators had the opportunity to exchange comments and to clarify issues in both the Investigators' Report and in the Health Review Committee's Commentary.

ambient air of Montreal, Quebec, were associated with daily all-cause and cause-specific mortality in the period 1984 to 1993 and (2) to determine whether groups of the population had higher than average risks of death from exposure to particles.

METHODS

Mortality and Particulate Matter

To achieve the first objective, the investigators obtained weather data from Dorval airport, air pollution data from Environment Canada, Montreal Urban Community, and the acid rain monitoring station in Sutton, Quebec (located 150 km southeast of Montreal), mortality data from the Quebec Minister of Health and Social Services, and health data from QHIP.

Weather data included airport visibility, barometric pressure, temperature, precipitation, relative humidity, and dew point. Airport visibility observations were converted to an extinction coefficient and used as a measure of particulate pollution. Available air pollution data included both measures of PM ($PM_{2.5}$, PM_{10}, total suspended particles [TSP], coefficient of haze [COH], and sulfate) and gaseous pollutants (CO, CO_2, NO, NO_2, and SO_2). Predicted daily levels of $PM_{2.5}$ were calculated from daily measures of COH, sulfate measured at the Sutton monitor (Sutton sulfate), and extinction coefficient. All PM measures were used by the investigators in their analyses; however, they presented in the main report only COH, predicted $PM_{2.5}$, and Sutton sulfate for effects on mortality. Results for the effects of other PM measures on mortality are presented in appendices available on request from the Health Effects Institute or from the HEI web site.

Underlying cause of death was coded according to the *International Classification of Diseases, Ninth Revision* (ICD-9), which is a system for numeric coding of specific conditions or groups of conditions. Analyses were conducted assuming several different temporal relationships between exposure and death (known as *lag* times). The main report shows analyses for the mean of 3 days' exposure—the average of exposures from the same day (lag 0), 1 day before death (lag 1), and 2 days before death (lag 2). Analyses of lag 0 and lag 1 effects on mortality were also conducted and the results included in appendices available on request from HEI or at the HEI web site. The percent change in mean number of daily deaths was calculated for each PM index for an increase equal to the interquartile range (IQR), referred to by the authors as the *mean percent change*. The IQR is the difference between the 25th and 75th percentile values of the distribution of daily mean pollutant values. Variables to control for the possible mortality effects of mean temperature and change in barometric pressure were included in the modeling.

The investigators examined the following specific causes of death for association with the three PM measures: cancers, cardiovascular diseases, coronary artery disease, respiratory diseases, digestive diseases, other nonaccidental causes (AIDS, diabetes, renal disease, and neurological conditions), and accidents. All analyses were also stratified by age (< 65 and ≥ 65).

Susceptible Groups

To accomplish the second study objective, identifying susceptible groups, the investigators developed a complex scheme for linking decedents to QHIP records to obtain information on health conditions up to 5 years before death. Nonaccidental deaths identified from the first part of the study were assigned to three sets of disease groups that the investigators developed: cancer, respiratory diseases, and cardiovascular diseases. Individuals with other medical conditions were combined into one group, and those who had no encounters with the medical system for a year before death were included in a no billing records group.

Each of the three disease groups included a number of conditions defined using QHIP billing records on medical services and procedures, diagnoses coded by physicians when submitting bills, and prescriptions filled by those over 65 years of age. Information for 2 months, 6 months, or 1 year before death was used, depending on whether the condition was acute or chronic.

The respiratory disease group included acute upper respiratory disease, chronic upper respiratory disease, acute lower respiratory disease, and airways disease. The cardiovascular disease group included acute coronary artery disease, chronic coronary artery disease, congestive heart failure, hypertension, cerebrovascular disease, and chronic rheumatic heart disease. The contributing criteria for each condition are in the Investigators' Report, Tables 17, 18, and 20. Analyses were also conducted for any coronary artery disease (acute coronary artery disease, chronic coronary artery disease, or congestive heart failure), any cardiovascular disease, and the group of individuals with no billing data in QHIP in the year prior to death.

Each defined disease included criteria that could be different for those < 65 and those ≥ 65, and included various combinations of the diagnosis using ICD-9 codes recorded by the physician for billing, prescriptions filled, services, tests, and procedures that might contribute to defining disease. If criteria were different between the two age groups, it was generally because prescription information was available for those over 65 years that could be used to define a condition.

MAJOR FINDINGS

Total and specific causes of death in the report are presented using a 3-day mean lag period for effects of the three measures of PM: COH, Sutton sulfate, and a predicted $PM_{2.5}$ estimate. The investigators observed an effect for each of the three PM measures on mortality for all nonaccidental causes, respiratory diseases, and diabetes (Commentary Table 1). They reported an effect for COH and predicted $PM_{2.5}$ of an approximate mean 2% change in nonaccidental mortality in Montreal, evaluated using 3-day mean exposure, across the IQR of the pollutant. The IQR for predicted $PM_{2.5}$ was 9.5 $\mu g/m^3$; for Sutton sulfate, 2.50 $\mu g/m^3$; and for COH, 1.85 (0.1 COH units/327.8 linear meters). Additionally, COH was associated with increases in cancer deaths, including specifically lung cancer deaths; Sutton sulfate was associated with mortality from coronary artery disease and cardiovascular diseases. Positive associations for other disease categories were not found. All associations were generally stronger among those 65 years of age and older.

The effects of the three particle measures varied somewhat by conditions that might confer susceptibility in each disease group (Commentary Table 2). All three measures were associated with acute lower respiratory disease, congestive heart failure, and the group including any cardiovascular disease. Associations with COH and predicted $PM_{2.5}$ were reported for cancer, chronic coronary artery disease, and any coronary artery disease; effects of sulfate were shown for acute and chronic upper respiratory disease. No associations with any of the three measures of PM were observed for airways disease, acute coronary artery disease, or hypertension.

Commentary Table 1. Causes of Death Positively Associated with Particulate Matter Measures

Cause of Death	COH	Sutton Sulfate	Predicted $PM_{2.5}$
Nonaccidental	+	+	+
Respiratory diseases	+	+	+
Diabetes	+	+	+
Lung cancer	+		
Cardiovascular diseases		+	
Coronary artery disease		+	

TECHNICAL EVALUATION

This is an impressive study, carefully executed, analyzed, and reported. Dr Goldberg and colleagues made efforts to identify sensitive populations using a unique database, in a population-based study. Many of the results agree with previous studies (see Tables 31 and 32) and add to the growing confirmation of the relationship of PM to daily mortality. As part of the review process, the HEI Health Review Committee discussed the issues below.

GASEOUS POLLUTANTS

The primary focus of this project was on the effects of PM, and the estimated effect of the gaseous pollutants was not addressed in this study. The role of the gaseous pollutants is important in interpreting the findings of time-series studies of PM. In this study, the PM effect was examined while controlling for the gaseous pollutants in the statistical models. A proposal by Dr Goldberg and his colleagues to examine the gaseous pollutant effects in this population has been approved for funding by HEI. It will be valuable to see estimates of effect for the gaseous pollutants as well, controlling for the presence of PM in the model, particularly since some recently published time-series studies report effects of the gaseous pollutants (Moolgavkar and Luebeck 1996; Burnett et al 1997).

Commentary Table 2. Susceptible Conditions Associated with Particulate Matter Measures

Condition[a]	COH	Sutton Sulfate	Predicted $PM_{2.5}$
Acute lower respiratory disease	+	+	+
Congestive heart failure	+	+	+
Any cardiovascular disease	+	+	+
Cancer	+		+
Chronic coronary artery disease	+		+
Any coronary artery disease	+		+
Acute upper respiratory disease		+	
Chronic upper respiratory disease		+	

[a] Conditions were defined using Quebec Health Insurance Plan data.

DEFINING SUSCEPTIBLE GROUPS

The HEI Health Review Committee thought that the criteria to define susceptible groups were generally reasonable, although some clinicians may not agree with some of the criteria. This approach is a good first step at moving beyond the use of death certificate diagnoses only, and toward considering medical conditions that might make individuals more susceptible to death. The Review Committee noted that definitions for a few of these conditions are such that apparent inconsistencies in the study findings emerged. Inconsistencies might also be expected by chance, since the investigators conducted a considerable number of analyses for three different lag periods, several PM measures, many causes of death, and many disease groups. Because inconsistencies may be meaningful, some are considered here.

One possible inconsistency centers on the definition of *airways disease*s and its reported associations with PM measures. Although mortality due to respiratory causes was strongly associated with each of the three measures of PM, individuals defined as having airways disease, which is a group of respiratory diseases, showed little or no increase in mortality associated with any of the three PM measures.

Considering *both* whether the method used to identify the airways disease group was valid, *and* whether the classification of the underlying respiratory cause of death was valid can be useful in evaluating the apparent inconsistency. A decedent was defined from QHIP records as having airways disease if a respiratory subspecialist made the diagnosis. If no respiratory subspecialist diagnosis was present, airways disease was defined by a general practitioner diagnosis, but only if at least two sequential lung function tests had been performed (see Table 17). In addition, for those ≥ 65, airways disease could be defined on the basis of only a prescription for a medication used primarily by patients with asthma or chronic obstructive pulmonary disease, with no requirement for physician diagnosis or lung function test. It is possible that this classification may have excluded many who did in fact have airways disease or, alternatively, include many who did not have it.

Misclassification resulting from the use of diagnostic billing codes is a possible explanation for these differences, given that the codes are assigned by physicians for the purpose of receiving reimbursement, although we have no way of knowing whether the impact of this on the findings would be significant or trivial. For example, a large effect of PM was observed when the airways disease group included only those at least 65 years old who were not prescribed one of the relevant medications for airways disease. Does this finding imply that misclassification was due to the prescription data? It would have been valuable to know the number of people in each of the disease groups broken down into the separate classification criteria. The findings with respect to this particular disease group appear to be sensitive to the method used to assign deaths to the group.

A puzzling, but interesting, finding was that increases in deaths due to diabetes were associated with increases in concentrations of all three PM measures. Since deaths caused directly by uncontrolled diabetes are now rare, and since contributing causes of death were not available from death certificates, one might speculate that diabetes deaths were associated with illnesses such as cardiovascular or renal disease; cardiovascular disease was associated with PM. Also, because of the relatively small number of deaths per day from diabetes (1 per day, on average), the finding must, as the investigators note, be interpreted cautiously. Yet, given the relatively high prevalence of diabetes in the population, it would be valuable to determine whether the risk of dying was highly associated with increases in PM for a group consisting of those with diabetes.

An interesting finding was that cancer deaths were also increased in association with increases in PM. As with diabetes, the acute cause of death in these individuals was not clear, since cancer patients succumb to a host of illnesses, including cardiovascular and respiratory diseases. A somewhat unexpected finding was the increased risk (for predicted $PM_{2.5}$ and sulfate) for individuals with no record of recent health billing, and for those not included in the cardiovascular disease, lower respiratory disease, or cancer groups.

These differences in findings between the mortality analysis and the susceptible groups analysis should be explored further. The investigators examined the effect of the three PM measures on each of the defined susceptible groups, but did not stratify by cause of death to determine whether those with the susceptible condition actually died from a cause that was associated with the PM measure. These findings also point to a cautious interpretation, with a need to replicate or explore further in the investigators' database.

EXPOSURE DATA

Measures for TSP, $PM_{2.5}$, and PM_{10} were available for every sixth day at a varying number of sites in and around Montreal, with sulfate levels determined from the collected samples. Continuous 2-hour integrated particle opacity measurements, COH, were obtained from 11 locations in Montreal, and daily total sulfate levels were obtained from the Sutton monitoring station. Because TSP and PM were not measured daily, the authors constructed

a linear regression model to predict daily $PM_{2.5}$ and used those predicted values in the health outcome models in order to provide more statistical power in the analysis (greater number of observations), since the measured values were limited. The predictive $PM_{2.5}$ model used measurements of COH, extinction coefficient (from airport visibility), and daily total sulfate from the Sutton monitoring station. A regression model is a reasonable approach; however, it should be accompanied by some method of accounting for the uncertainty in the regression-based predictions (both the uncertainty of the parameter estimate and the residual error).

The extinction coefficient, a measure of particle and gaseous light scattering and absorption, is not independent of sulfate or COH, which is strongly associated with carbon aerosol, and both reduce visibility. Use of the extinction coefficient, COH, and Sutton sulfate values to predict daily $PM_{2.5}$ may be a potentially important source of misclassification in the predicted daily $PM_{2.5}$ concentrations.

Airport visibility observations are available from airports throughout North America, with observations going back several decades in many locations. When corrected, as the authors did in this study, airport visibility observations might serve as reasonable historical measures of fine PM. The authors chose not to use the extinction coefficient as a metric of fine particle exposure in the health models described in the Investigators' Report because of the considerable uncertainty in the calculation of the extinction coefficient from airport visibility observations; however, these results are presented in Appendix E.

The investigators reported Pearson correlation coefficients to be approximately 0.9 between total sulfate measured at the Sutton station and sulfate measured from $PM_{2.5}$ at the two monitoring stations in Montreal. The sulfate values measured at the Sutton site appear to be excellent indicators of regional sulfate concentrations.

In a substudy, the authors demonstrated the strong relation between COH and carbon particles, particularly elemental carbon. Correlations among COH concentrations at 11 sites in Montreal showed considerable variability, from 0.2 to 0.7, which suggests that substantial spatial heterogeneity exists in the COH exposure metric, and that a simple averaging of values from different stations to represent regionwide daily averages may introduce exposure misclassification. This spatial variability was further documented in a small substudy conducted by the authors. Becasue it was not possible to assign individuals COH exposure values obtained from monitors close to their home addresses because of the lack of time-activity information, as with other time-series studies, using a single regional exposure should be recognized as a limitation in the study.

CONCLUSIONS

Dr Goldberg and his colleagues have made a unique effort to address some of the limitations of mortality outcomes that have been used in most earlier studies of air pollution and daily mortality. Their study has advanced current methods and scientific understanding in several ways.

1. They have demonstrated the feasibility of using the substantial resources offered by a national health insurance database, linking the information to mortality and air pollution data to study the epidemiology of air pollution and mortality.
2. They have developed methods based on computer-intensive technology for using such databases in conjunction with expert clinical judgment that they, as well as others, can apply to future research.
3. They have provided results suggesting that persons with certain preexisting cardiac or respiratory conditions are at short-term increased risk of mortality due to ambient particles. Observed differences between results using case definitions based on the QHIP data and those based on death certificate data should be more thoroughly explored.
4. They have identified other clinical conditions that may be associated with increased risk of mortality. In particular, the investigators identified persons with cancer and diabetes as being at increased risk of death, as well as those with no billing records in the year before death. These results warrant further investigation.
5. Further analyses with this data set could advance understanding of who might be at greatest risk of mortality at levels of air pollution currently observed in the cities of the developed world. Using the information in this database in conjunction with statistical methods to remove effects of mortality displacement could also be useful in advancing our understanding of this issue.

ACKNOWLEDGEMENTS

The Health Review Committee thanks Dr Diane Mundt for help in preparing the Commentary; and John Abbott, Julia Campeti, Sally Edwards, Virgi Hepner, Joanne Merriman, and Quentin Sullivan in preparing the Research Report for publication.

REFERENCES

Anderson HR. 1999. Health effects of air pollution episodes. In: Air Pollution and Health (Holgate S, Samet J, Koren H, Maynard R, eds). Academic Press, Orlando FL.

Bates D. 1994. Discussion paper presented at an HEI particle research planning workshop, Berkeley CA, April 15, 1994. Health Effects Institute, Cambridge MA.

Brunekreef B, Hoek G. 2000. Beyond the body count: Air pollution and death. Am J Epidemiol 151(5):449–451.

Burnett RT, Cakmak S, Brook J, Krewski D. 1997. The role of particulate size and chemistry in the association between summertime ambient air pollution and hospitalization for cardio-respiratory diseases. Environ Health Perspect 105:614–620.

Goldberg MS. 1996. Particulate air pollution and daily mortality: Who is at risk? J Aerosol Med 9:43–53.

Lyon JL, Mori M, Renlu G. 1994. Daily mortality and exposure to PM_{10} air pollution, Utah County, Utah, 1985–1992. Presentation at the Colloquium on Particulate Air Pollution and Human Mortality and Morbidity, January 24, 1994, Irvine CA.

Moolgavkar SH, Luebeck EG. 1996. A critical review of the evidence on particulate air pollution and mortality. Epidemiology 7:420–428.

Pope CA III, Dockery DW. 1999. Epidemiology of particle effects. In: Air Pollution and Health (Holgate S, Samet J, Koren H, Maynard R, eds). Academic Press, Orlando FL.

Samet JM, Zeger SL, Dominici F, Curriero F, Coursac I, Dockery DW, Schwartz J, Zanobetti A. 2000. The National Morbidity, Mortality, and Air Pollution Study, Part II: Morbidity, Mortality, and Air Pollution in the United States. Research Report 94. Health Effects Institute, Cambridge MA.

Schwartz J. 1994. What are people dying of on high air pollution days? Environ Res 64:26–35.

Schwartz J. 2000. Harvesting and long-term exposure effects in the relationship between air pollution and mortality. Am J Epidemiol 15:440–448.

Utell MJ, Samet JM. 1993. Particulate air pollution and death, new evidence on an old problem [editorial]. Am Rev Respir Dis 147:1334–1335.

Zeger SL, Dominici F, Samet J. 1999. Harvesting-resistant estimates of air pollution effects on mortality. Epidemiology 10:171–175.

RELATED HEI PUBLICATIONS: PARTICULATE MATTER

Report Number	Title	Principal Investigator	Publication Date*
Research Reports			
40	Retention Modeling of Diesel Exhaust Particles in Rats and Humans	CP Yu	1991
45	The Effects of Exercise on Dose and Dose Distribution of Inhaled Automotive Pollutants	MT Kleinman	1991
68	Pulmonary Toxicity of Inhaled Diesel Exhaust and Carbon Black in Chronically Exposed Rats		
	Part I. Neoplastic and Nonneoplastic Lung Lesions	JL Mauderly	1995
	Part II. DNA Damage	K Randerath	1995
	Part III. Examination of Possible Target Genes	SA Belinsky	1995
75	Ozone Exposure and Daily Mortality in Mexico City: A Time-Series Analysis	DP Loomis	1996
83	Daily Changes in Oxygen Saturation and Pulse Rate Associated with Particulate Air Pollution and Barometric Pressure	DW Dockery	1999
86	Statistical Methods for Epidemiologic Studies of the Health Effects of Air Pollution	W Navidi	1999
91	Mechanisms of Morbidity and Mortality from Exposure to Ambient Air Particles	JJ Godleski	2000
93	Effects of Concentrated Ambient Particles in Rats and Hamsters: An Exploratory Study	T Gordon	2000
94	The National Morbidity, Mortality, and Air Pollution Study	JM Samet	2000
	Part I. Methods and Methodologic Issues		
	Part II. Morbidity and Mortality from Air Pollution in the United States		
95	Association of Particulate Matter Components with Daily Mortality and Morbidity in Urban Populations	M Lippmann	2000
96	Acute Pulmonary Effects of Ultrafine Particles in Rats and Mice	G Oberdörster	2000
98	Daily Mortality and Fine and Ultrafine Particles in Erfurt, Germany	H-E Wichmann	2000
	Part I. Role of Particle Number and Particle Mass (In press)		
99	A Case-Crossover Analysis of Fine Particulate Matter Air Pollution and Out-of-Hospital Sudden Cardiac Arrest (In press)	H Checkoway	2000

Continued

** Reports published since 1990.*
Copies of these reports can be obtained by contacting the Health Effects Institute, 955 Massachusetts Avenue, Cambridge, MA 02139. Phone (617) 876-6700 FAX (617) 876-6709 E-mail pubs@healtheffects.org www.healtheffects.org

RELATED HEI PUBLICATIONS: PARTICULATE MATTER

Research Reports

Report Number	Title	Principal Investigator	Publication Date*
Special Reports			
	Particulate Air Pollution and Daily Mortality: The Phase I Report of the Particle Epidemiology Evaluation Project		
	Phase I.A. Replication and Validation of Selected Studies		1995
	Phase I.B. Analyses of the Effects of Weather and Multiple Air Pollutants		1997
	Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality: A Special Report of the Institute's Particle Epidemiology Reanalysis Project		2000
HEI Communications			
5	Formation and Characterization of Particles: Report of the 1996 HEI Workshop		1997
8	The Health Effects of Fine Particles: Key Questions and the 2003 Review		1999
HEI Program Summaries			
	Research on Particulate Matter		1999

** Reports published since 1990.*
Copies of these reports can be obtained by contacting the Health Effects Institute, 955 Massachusetts Avenue, Cambridge, MA 02139. Phone (617) 876-6700 FAX (617) 876-6709 E-mail pubs@healtheffects.org www.healtheffects.org

HEALTH
EFFECTS
INSTITUTE

955 Massachusetts Avenue
Cambridge MA 02139 USA
+1-617-876-6700
www.healtheffects.org

RESEARCH
REPORT

Number 94, Part I
May 2000