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The relationship between short-term exposure to gaseous air pollutants and cardiovascular morbidity and mortality in the elderly population in Vancouver, British Columbia

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The relationship between short-term exposure to gaseous air pollutants and cardiovascular morbidity and mortality in the elderly population in Vancouver, British Columbia

by

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ABBREVIATIONS

AIC	Akaike's Information Criteria
AMI	Acute myocardial infarction
BC	British Columbia
Cardio	Cardiovascular
CI	Confidence interval
CO_2	Carbon monoxide
COH	Coefficient of haze
°C	Degrees Celsius
df	Degrees of freedom
GEE	Generalized estimating equation
GVRD	Greater Vancouver Regional District
H^+	Aerosol acidity
HF	Heart failure
ICD9	International Classification of Disease, Ninth Revision
IHD	Ischemic heart disease
IQR	Interquartile range
LOESS	Locally weighted regression
min	Minimum
max	Maximum
MPC	Mean percent change
NAAQO	National ambient air quality objectives
NMMAPS	National, Morbidity, Mortality and Air Pollution Study
NO_2	Nitrogen dioxide
O_3	Ozone
PM	Particulate matter
$PM_{2.5}$	Particulate matter with an aerodiameter of <= 2.5 µm
PM_{10}	Particulate matter with an aerodiameter of <= 10 µm
ppb	Parts per billion
ppm	Parts per million
PPV	Positive predictive value
RR	Relative risk
SD	Standard deviation
SO_2	Sulphur dioxide
TEOM	Tapered-element oscillating microbalance
TSP	Total suspended particulates

ABSTRACT

The present study investigated the association between gaseous air pollutants and mortality and morbidity due to specific cardiovascular conditions in the elderly population in Vancouver, British Columbia. Time-series analysis was utilized to evaluate the daily levels of carbon monoxide (CO), nitrogen dioxide (NO_2), sulphur dioxide (SO_2), and ozone (O_3) in relation to cardiovascular hospital admissions and deaths between January 1985 and March 1999. Results showed significant associations between CO and ischemic heart disease and heart failure admissions, NO_2 and all cardiovascular hospitalizations and stroke deaths and between SO_2 and heart failure hospital admissions. Vancouver air pollutant levels were well below the Canadian National Ambient Air Quality Objectives maximum acceptable levels. However the results of this study showed a negative influence on the population's health suggesting that a re-evaluation of these standards may be necessary.

1. CHAPTER 1 INTRODUCTION

1.1. General

In Canada, cardiovascular disease is the leading cause of death. Over a third of deaths are attributed to cardiovascular conditions, with ischemic heart disease accounting for the largest percentage of deaths (20%). Along with being the leading cause of death within Canada cardiovascular disease is the leading cause of hospitalization (excluding childbirth).(1) In 2000-2001, 21% of all hospitalizations for men and 15% of hospitalizations for women were attributed to cardiovascular diseases. The number of cases of cardiovascular disease is predicted to increase over the next 20 years because of the aging of the population. According to 2001 Canadian Census data 13% of the population was 65 years of age or older. This proportion is projected to increase to 15% by 2011 and to over 20% by 2025.(2)

According to Health Canada's 1998 Economic Burden of Illness in Canada, the cost of illness in Canada is approximately $159.4 billion per year. Of this total expenditure, cardiovascular disease is the most costly diagnostic category at over $18 billion a year. Components of the costs include direct expenditures (over $6 billion) such as hospital care, drugs, physician care and research along with indirect costs (over $11 billion) such as expenses due to short and long-term disability.(3)

Although lifestyle and genetic factors and the health care system influence cardiovascular and overall health, environment factors (social, physical or economic) are important additional health determinants.(4) Air pollution has been recognized as

influencing the health of Canadians and the National Ambient Air Quality Objectives were developed in part to protect Canadians' health.(5)

The need for air is a constant requirement. An average person takes approximately 10 million breaths a year.(6) The World Health Organization and the Greater Vancouver Regional District (GVRD) suggest that clean air is a basic human right.(6, 7) The GVRD is a partnership of 21 municipalities and an electoral area that comprise the metropolitan area of Greater Vancouver. Their role is to deliver essential utility services and protect and enhance the quality of life in Greater Vancouver. Air quality in Vancouver is relatively good compared to other major cities in North America; however, the GVRD predicts that emissions will increase in the next 15 to 20 years due to an increase in the population, international trade and transportation. Without action, air quality will decline.(8-10) In response to this, in October 2005 the GVRD released the Air Quality Management Plan which outlined three primary goals: minimize the risk to public health from air pollution, improve visibility, and minimize Greater Vancouver's contribution to global climate change.(10)

In comparison to other Canadians, British Columbians are generally healthy. The Canadian Institute for Health Information reported that British Columbia (BC) had the highest life expectancy at birth (80.4 years) out of all the Canadian provinces and territories.(11) Compared to national statistics, BC had a lower prevalence of adults with each reported modifiable risk factor (daily smoking, physical inactivity, overweight, less than recommended consumption of fruits and vegetables, high blood pressure or diabetes) for cardiovascular disease.(2) In 2004-2005 BC was the province with the

lowest age-standardized rate of new stroke and acute myocardial infarction (AMI) hospitalizations.(12) Furthermore, the Heart and Stroke Foundation reported that cardiovascular mortality rates were the lowest for BC, Nunavut, and the Northwest Territories during the period between 1995 and1999.(2)

Vancouver, BC was selected for this study because it is a large urban centre with a generally health population and low gaseous air pollutant levels. If an association between air pollution and hospital admissions or death can be demonstrated at levels well below the National Ambient Air Quality Objectives, this would suggest that air pollution may still pose a public health risk even under the stringent guidelines. Conversely, for any of the pollutants under investigation it is unclear whether a threshold concentration exists below which no health effects are observed.

It was estimated that health care costs due to air pollution in the Lower Fraser Valley would reach $1 billion annually.(13) The BC Ministry of Health estimated that between 120 and 400 premature deaths per year could be attributed to air pollution with half due to outdoor air pollution. Furthermore, between 700 and 2,000 hospital admissions and between 900 and 2,700 emergency room visits could be attributed to air pollution.(13) The health effect of air pollution is relatively small, but the health impact to the population can be considerable given the breadth of exposure.

1.2. Research Objectives

It is hypothesized that short-term exposure to gaseous air pollutants is associated with increased risk of cardiovascular hospitalizations and deaths. Given that the elderly are at risk for cardiovascular issues, the percentage of deaths due to cardiovascular

conditions increase with age and older age groups are at higher risk of mortality associated with air pollution, the study was restricted to those 65 years and older. (1, 14)

Overall objective:

- To evaluate the relationship between daily levels of gaseous air pollutants and mortality and morbidity due to cardiovascular conditions in the elderly population in Vancouver, British Columbia using time-series analysis

Secondary objectives:

- To assess the association of gaseous air pollutants with specific cardiovascular conditions in Vancouver
- To assess the impact of using different lag periods on relative risk estimates
- To evaluate the possible impact of warm and cool seasonality on the estimated risk of ozone

1.3. Cardiovascular disease

Cardiovascular diseases are conditions affecting the cardiovascular system. This includes the heart and its blood vessels, and the system of veins and arteries throughout the body and brain. Stroke is also considered a form of cardiovascular disease and is the result of a blood flow problem with the brain.(15)

1.3.1. Stroke

A stroke occurs when there is an interruption of the normal blood flow to the brain. Blood vessels of the brain may rupture or become blocked by a clot. Without oxygen from a normal blood flow, brain cells may become damaged or die potentially leading to

loss of consciousness, sensation or dizziness. A stroke can affect, among other things, a person's senses, motor skills or ability to communicate.(16-18) Canadian stroke hospitalization rate data varied between the 1980s and 1990s; however, it is estimated that future rates will follow the increasing trend seen in the 1980s.(2)

1.3.2. Ischemic heart disease (IHD)

Ischemic heart disease is a condition that occurs when the heart does not receive enough blood and oxygen. The heart muscle becomes damaged or works inefficiently when the blood flow is reduced or absent. Angina, or chest pain, may occur if blood flow is partially blocked and myocardial infarction is a risk if blood flow is suddenly completely blocked from the heart.(2, 18) IHD hospitalizations have been increasing in Canada since 1980 and are predicted to continue with the increase projected to be much higher for men than for women.(2)

1.3.3. Acute myocardial infarction (AMI)

Acute myocardial infarction (AMI), commonly known as a heart attack, is a specific type of ischemic heart disease where the blood supply to the heart is severely restricted or blocked leading to the death of part of the cardiac muscle.(1, 2) The majority of AMIs (over 90%) are caused by a blood clot in the arteries supplying blood to the heart. Symptoms vary including chest pain, sweating and shortness of breath.(19, 20) The incidence of AMI, as well as the case fatality rate, increases with age.(20) Canadian hospitalization data reported, approximately 11.1% of AMI patients admitted to hospital between 2002-2003 and 2004-2005 died within 30 days.(12) In Canada, AMI hospitalizations have been increasing since 1980 and if a individual is hospitalized for AMI it is usually the primary determinant of the length of the hospital stay.(2)

1.3.4. Heart failure

Heart failure occurs when the heart cannot pump effectively enough to meet the body's needs.(2, 21) Heart failure generally occurs because of damage to the heart muscle but may also be due to increased demands on the heart. When the heart cannot pump blood through the body efficiently, oxygen and nutrient levels are reduced. The incidence of heart failure increases with age and is associated with high morbidity and mortality.(22) According to data from the Hospital Morbidity Database at the Canadian Institute for Health Information, heart failure is generally a co-morbid condition rather than the primary reason for an individual's hospitalization. Hospitalizations have increased, stabilized, and decreased since the 1980s; however, an increase is predicted in the future.(2)

1.3.5. Cardiovascular risk factors

Major risk factors for cardiovascular conditions include: smoking, high blood pressure, elevated serum total and low-density lipoprotein (LDL) cholesterol, low serum high-density lipoprotein (HDL) cholesterol, diabetes and age.(2, 23) Studies specifically concentrating on the elderly population have reported a similar set of risk factors. The Framingham Heart Study found that total cholesterol was a primary risk factor for heart disease.(24) An American prospective study reported that five important independent predictors of heart failure in the elderly are male sex, older age, diabetes, pulse pressure and body mass index.(25) Although air pollution is not a traditionally reported cardiovascular risk factor, in 2004 the American Heart Association released a statement to raise concerns about air pollution and its effects on cardiovascular health.(26)

1.3.6. Canadian cardiovascular morbidity and mortality trends

Cardiovascular diseases are the leading cause of death within Canada and, excluding childbirth, are the leading cause of hospitalization. In 2000-2001 cardiovascular hospitalizations accounted for over 20% of hospitalizations for men and 15% for women, excluding admissions for childbirth and pregnancy. The number of cardiovascular hospitalizations increased between 1979 and the middle of the 1990s and then stabilized in the latter part of the 1990s. Cardiovascular hospitalizations increase with age and although rates for all cardiovascular diseases except congestive heart failure are decreasing, it is projected that the actual number of hospitalizations will increase as the population ages.(2)

One in three Canadians had a cardiovascular disease as their underlying cause of death. In 1999, after cancer (29%), ischemic heart disease accounted for the largest percentage of deaths (20%). Furthermore, acute myocardial infarction accounted for half of the ischemic heart disease deaths. Cerebrovascular diseases, mainly stroke, accounted for seven percent of the overall deaths. Although cardiovascular mortality rates were decreasing during the 1990s the actual number of cardiovascular deaths has remained stable due to the increase in the elderly age group within the Canadian population. Using statistics from the mid to late 1990s, in comparison to other countries, Canada was ranked fourth behind Japan, France and Spain for lowest reported cardiovascular mortality rate.(2)

1.4. Gaseous air pollution

Major gaseous air pollutants include carbon monoxide (CO), nitrogen dioxide (NO_2), sulphur dioxide (SO_2) and ozone (O_3).

1.4.1. Carbon Monoxide (CO)

Carbon monoxide is a colourless, odourless, but toxic gas.(27) It is formed by the incomplete combustion of fuels that contain carbon.(28) Vehicle exhaust is the most common outdoor source of CO and in the Lower Fraser Valley of Greater Vancouver it accounts for 90% of the CO pollution.(27, 29)

Carbon monoxide's health effects may be due in part to hemoglobin and myoglobins' affinity for CO. During the normal functioning of the body, oxygen attaches to hemoglobin and is delivered to the peripheral tissues of the body. However, hemoglobin's affinity for CO is 200 to 250 times stronger than its affinity for oxygen. Myoglobin is a similar oxygen-binding protein to haemoglobin, but it is found in the heart. Experimental studies have suggested that the binding of CO to myoglobin can reduce the functioning of the cardiac muscles.(30) When CO binds to hemoglobin or myoglobin the result is decreased oxygen-carrying capacity and impaired storage and release of oxygen in the body.(27, 31) Additionally, models have shown decreased myoglobin concentrations in persons with heart disease, implying that these individuals have decreased oxygen-carrying capacity. Therefore, those already at risk for cardiac events may be more susceptible to CO exposure than healthy individuals.(31) In a study examining the association between air pollution and hospitalization of elderly for congestive heart failure conditions, it was found that CO was the strongest predictor of

hospitalization and the least sensitive to adjustments for seasonal, subseasonal and weekly cycles of hospital usage.(32)

Common acute symptoms of CO inhalation include headache, dizziness, weakness, nausea, difficulty in concentrating, shortness of breath, and visual changes. Symptoms reported less frequently include chest pain, loss of consciousness, abdominal pain and muscle cramping.(33) Severe symptoms of CO poisoning include angina, seizures, respiratory depression and coma.(34)

1.4.2. Nitrogen Dioxide (NO_2)

Nitrogen dioxide and nitric oxide are both generated during the combustion of fossil fuels. Larger quantities of nitric oxide rather than nitrogen dioxide are produced; however, nitric oxide rapidly reacts in the atmosphere to produce nitrogen dioxide. Along with being a gaseous pollutant of concern, NO_2 reacts in the presence of sunlight and volatile organic chemicals to form ozone.(28, 29) Nitrogen dioxide is acknowledged as a good indicator of vehicle air pollution since combustion emissions, primarily from vehicle exhaust produce nitrogen oxide.(30)

In a study of non-accidental death and air pollution in 11 Canadian cities, it was found that nitrogen dioxide had the largest effect on mortality, followed by ozone, sulphur dioxide and carbon monoxide.(35) According to von Klot et al., NO_2 has "no known effect on the cardiovascular system".(36) However, a study of 83 patients by Chan et al. demonstrated that environmental exposure to NO_2 was associated with reducing heart rate variability (HRV) and suggested that the findings support the theory that "a decrease in HRV has been shown to be a predictor of increased mortality after a myocardial

infarction and has been related to sudden arrhythmic death".(37) A study of 20 healthy volunteers found that exposure to NO_2 led to a significant decrease in the number of red blood cells and hemoglobin concentration. The study also found a decrease in the number of white blood cells; however, this association was not statistically significant. The investigators acknowledged that the decrease in blood cell counts was small and likely not clinically significant for most individuals; however, it may impact more susceptible populations such as the very young, the elderly or those who have pre-existing cardiovascular or respiratory conditions.(38)

1.4.3. Sulphur Dioxide (SO_2)

Sulphur dioxide is a pungent, colourless gas that is formed during the combustion of fossil fuels containing sulphur. These types of fossil fuels are generally used for home heating or power generation. In the Fraser Valley, the levels of sulphur dioxide are low compared with other cities of similar size because most industries and residents utilize natural gas rather than sulphur-containing fossil fuels coal and oil.(28, 29) The largest contributors of SO_2 to the Fraser Valley are marine vessels and the petroleum products industry.(39)

Short-term exposure can lead to bronchoconstriction resulting in wheezing or shortness of breath.(30) Individuals exposed to high levels of sulphur dioxide may experience "respiratory illness, alterations in pulmonary defences or aggravation of existing cardiovascular disease." Those at higher risk for the adverse health effects of sulphur dioxide include children and the elderly, and those with chronic conditions such as asthma and cardiovascular or lung disease.(28)

1.4.4. Ozone (O_3)

According to the World Health Organization (WHO) "ozone is the most important photochemical oxidant in the troposphere."(40) Unlike the other previously discussed pollutants, ozone is not an emitted pollutant.(5) Ozone is formed through a set of reactions involving sunlight, nitrogen dioxide and hydrocarbons. Due to its photochemical properties, ozone levels are strongly influenced by seasonality. Ozone levels are generally the highest after multiple hot, sunny days.(28) In addition to seasonal variation, ozone levels vary by geography. Levels are generally lower in urban areas compared to suburban or rural areas. This is due to the scavenging of ozone by nitric oxide produced from emissions.

The majority of health effects studied focused on respiratory issues. According to the WHO, health effects include "...respiratory symptoms, pulmonary function changes, increased airway responsiveness and airway inflammation."(30) Laboratory ozone studies have observed "upper respiratory irritation, cough, shortness of breath, wheezing, decreased tidal volume, nausea, malaise and headache".(28) Inconsistent study results have been reported for the relationship between ozone and cardiovascular disease. In a study completed in Detroit, Michigan, ozone was not associated with admissions for cardiovascular disease.(41) Conversely, ozone was associated with a significant increase in all-cause, cardiovascular and respiratory mortality in London.(42) A review of several short-term ozone studies found that almost all of the studies reported a positive association with ozone; however, upon further scrutiny the reviewers reportedly found questionable statistical analyses and a lack of consideration for potential confounders.(43)

1.4.5. Gaseous air pollution trends

The National Ambient Air Quality Objectives (NAAQO) were initially developed in the mid-1970s and are intended as benchmarks for Canada to assess air quality.(5) Individual provinces and regional jurisdictions have the option to develop more stringent objectives based on local need; however, Vancouver utilizes the national objectives as their benchmark.

Table 1.1 Canadian National Ambient Air Quality Objectives (5, 44)

Pollutant	Averaging Period	Maximum Acceptable Level
Carbon monoxide	8 hours	13 ppm
Nitrogen dioxide	24 hours	160 ppb
Sulphur dioxide	24 hours	115 ppb
Ozone	1 hour	82 ppb

Vancouver has relatively good air quality compared to other urban North American cities. Gaseous air pollution levels in Vancouver were relatively low compared to the maximum acceptable levels specified by Canada's National Ambient Air Quality Objectives.(9, 29) Short-term peak (99^{th} percentile of the 1-hour values) and average levels of NO_2 and CO have declined by large margins in the Lower Fraser Valley since 1988 (NO_2 by more than 25% and CO by more than 40%). Similarly, short-term peak and average levels of SO_2 have declined since 1988. Sulphur dioxide levels in the Lower Fraser Valley have been very low compared to the national objectives. Short-term peak ozone levels have

also declined between 15% and 20% since the late 1980s; however, average levels have increased slightly.(29)

1.5. Epidemiological studies on the short-term effects of gaseous air pollution on cardiovascular hospitalization and mortality in the elderly

1.5.1. Recent studies

Cardiovascular specific hospitalization and mortality

Recently there has been increased interest in the association between gaseous air pollution and cardiovascular conditions. It has been suggested that there is a stronger association between air pollution and cardiovascular conditions compared to all causes or respiratory conditions.(14, 45, 46) Hoek et al. suggested that specific cardiovascular causes of death, particularly heart failure, are more strongly associated with air pollution than total cardiovascular mortality.(47) Another study found significant associations of O_3, SO_2 and NO_2 with mortality due to ischemic heart disease while no association was found for all-cause mortality or cardiovascular conditions.(48)

Stroke

Few studies have investigated the association between gaseous air pollutants and daily stroke hospitalizations. A Hong Kong study found no association between gaseous air pollutants (SO_2, NO_2, and O_3) and hospital admissions for cerebrovascular conditions, which include stroke.(49) Specifically investigating stroke, a multi-city European study reported a non-significant association between SO_2 and stroke admissions.(50) In contrast, a study in Helsinki reported a significant association between NO_2 and hospital admissions for cerebrovascular conditions.(51)

For stroke mortality, two Korean studies reported a significant relationship between stroke mortality and all four gaseous pollutants.(52, 53) Furthermore, one of the studies reported the effect size of the gaseous pollutants on stroke mortality was greater than that of PM_{10}.(52) A Netherlands study also found a significant associated between gaseous pollutants (O_3, CO, SO_2) and cerebrovascular mortality.(47) In contrast, Kan et al. reported that NO_2 but not SO_2 was significantly associated with stroke mortality in Shanghai, China.(54) And a study in Hong Kong found that neither of the gaseous pollutants examined (SO_2, NO_2) were significantly associated with stroke mortality.(48) It is important to note that these studies only presented results from single or 2-pollutant models while the non-significant association reported by Kan et al. was adjusted for other pollutants.

Ischemic heart disease (IHD)

Heart disease hospitalizations were significantly associated with NO_2 and O_3, the two gaseous pollutants being examined, with one study reporting the largest effect in the 65 and greater age group.(51, 55) In a separate study, specifically focusing on those 65 years and older, SO_2 and CO were significantly associated with ischemic heart disease admissions in single pollutant models, while O_3 was not. However, after controlling for other pollutants, SO_2 and CO became insignificant.(41) Another SO_2 specific study found similar single and multiple pollutant model results (50) while a Hong Kong study reported no association between ischemic heart disease admissions and any of the pollutants under investigation(NO_2, SO_2, O_3).(49) A study completed by a subset of the authors

from the Hong Kong hospitalization study, found a significant association between ischemic heart disease deaths and NO_2, SO_2, O_3 when modelled individually.(48)

Acute myocardial infarction (AMI)

Few studies have been published specifically examining acute myocardial infarction and gaseous air pollutants. In one case-crossover study, O_3 was found to be significant in relation to AMI events (death or morbidity) while NO_2 and SO_2 were not.(56) In an Italian case-crossover study, results showed positive and significant associations of NO_2 and CO with AMI hospitalizations.(57) Another study that combined myocardial infarction with other ischemic heart disease deaths reported non-significant associations with all gaseous pollutants.(47) All of these studies reported single-pollutant model results.

Heart failure

There have been few Canadian studies that have examined the relationship between gaseous pollutants and specific cardiovascular hospitalizations or mortality. Burnett et al. studied the effects of air pollution on hospitalization for heart failure in the elderly in 10 Canadian cities including Vancouver. The results of the study showed a positive association of hospitalization with CO, NO_2 and SO_2, but not with O_3.(32) An American multi-city study and one specific to Detroit, Michigan also reported a significant association between CO and heart failure admissions among the elderly but did not find a consistent, positive association with the other gaseous pollutants.(41, 45) In contrast, a Hong Kong study reported a significant association of heart failure admissions with SO_2, NO_2 and O_3. Carbon monoxide was not examined as part of the Hong Kong

study.(49) And a study completed in the Netherlands reported a statistically significant relationship between all four gaseous pollutants and heart failure mortality.(47)

1.5.2. Methodological issues

The majority of air pollution studies have focused on short-term effects of air pollution and have been conducted using a time-series approach. Time-series analysis utilizes administrative data to investigate the association of air pollution and hospitalization or mortality by studying the short-term changes in air pollution levels along with the short-term changes in hospitalization or mortality. Regression modeling in time-series analysis allows for adjustments of the potential confounding effects of seasonality, trends and weather.(58) In a comparison of time-series and case-crossover analyses, Fung et al. found that accurate estimates can be determined with both methods; however, both require decisions to be made by the researcher. The final recommendation of the study favoured an analysis approach using time-series due to the fact that more precise estimates can be determined using the best time-series methodologies in comparison to the best case-crossover study design.(59) According to Tsai, case-crossover and time-series approaches produce "almost identical results".(60)

Research of methodological issues in time-series analysis is leading to more accurate exposure-outcome models and estimates of relative risks. Dominici et al. reported that past studies using default convergence parameters with the generalized additive model (GAM) in S-Plus overestimated the relative risks. Analysis should control convergence parameters. Dominici et al. also found that the bias in the relative risk estimates is larger when locally weighted regression (LOESS) smoothers are used compared to splines.(58) Furthermore, Ramsay et al. found that if concurvity is an issue, natural

spline smoothing functions will result in more accurate estimates of relative risks and their standard errors.(61)

A cohort or controlled environment study would not have been feasible for this investigation; however time-series analysis is a viable alternative to contribute evidence to the arena of cardiovascular disease and air pollution. Burnett et al. reported that under specific conditions population relative risk estimates from time-series studies are equivalent to estimates of an individual's life lost obtained from cohort studies.(62) Furthermore, results from an epidemiological study, versus a controlled environment study, may be generalized to a broader population. However, there is a possibility of bias due to measurement error given the study's assumption that air pollution levels from monitoring stations represent personal exposure levels. There is also a risk of misclassification of the exposure or outcome variables under investigation.

Investigators comparing different analytical methods have found relatively consistent results even when different time-series modelling techniques were employed. Models included different forms of weather and pollution specifications, different assumptions about lag times between levels of pollution and mortality and different assumptions about the dependence of mortality on previous days mortality counts.(63) A Health Effects Institute study examined the association between air pollution and daily mortality using three different statistical models to control for the effects of weather. The first model used summary categories of weather variables to describe daily weather patterns. A second model incorporated a mathematical equation of the temporal relationship between mortality and the previous day's absolute and dew-point temperature. The final

model incorporated the current and previous day's absolute and dew-point temperature along with indicator variables for hot and cold days. The study found that the different approaches to characterizing weather variables did not substantially influence the observed association between air pollution and mortality. Furthermore, the investigators could not find patterns within the estimates derived from the three models.(64) However reviewing published studies, a variety of inconsistent results have been reported under various population and environmental conditions. Table 1.2, 1.3 and 1.4 provide a summary of recent short-term air pollution and cardiovascular studies.

Table 1.2 Summary of recent short-term gaseous pollutant and hospital admission studies

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Ruidavets et al. (2005) > Location: Toulouse, France > Study period: Jan 1, 1997, to Jun 30, 1999 (56)4)	Acute myocardial infarction event (death or morbidity)	NO_2, SO_2, and O_3 (0-3)	Case-crossover, conditional logistic regression	Temperature, humidity, and influenza epidemics	> Association between O_3 (same day and previous day) and AMI	> Single pollutant model results reported
D'Ipolitti et al. (2003) > Rome, Italy > Jan 1995 to Jun 1997 (57)5)	Acute myocardial infarction and heart failure	TSP, CO, NO_2, and SO_2 (0-4 and cumulative 0-2 days)	Case-crossover, conditional logistic regression	Temperature, humidity, barometric pressure	>Association with AMI and same-day NO_2 > Association with 2-day lag CO and with cumulative lag	> Single pollutant model results reported

Table 1.2 Summary of recent short-term gaseous pollutant and hospital admission studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Sunyer et al. (2002) > 7 European areas > 1985 to 1990 (50)8)	Cardiovascular admissions including stroke and heart disease specifically (population divided into over and below 65 years of age)	SO_2 (0-3)	Time-series, Poisson auto regression, generalized additive models	Temperature, humidity, holiday periods, influenza episodes, PM_{10}, CO, NO_2, O_3	> Association between cardiovascular admissions and SO_2 > Association between IHD admissions for those > 65 and SO_2 (single pollutant model) > Associations became non-significant when adjusted for the other pollutants	> Pollutant levels were determined based on in-city monitoring stations, stations near highways were excluded > Specific effects of each pollutant not investigated > Heterogeneous results across the areas explained by different levels of humidity; estimates were stronger at lower levels of humidity

Table 1.2 Summary of recent short-term gaseous pollutant and hospital admission studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Wong et al. (2002) > London (1992 to 1994) and Hong Kong (1995 to 1997) (65)3)	Cardiovascular and IHD admissions year-round and by warm/cool season	PM_{10}, NO_2, SO_2, O_3 (0-3)	Time-series, Poisson regression, degree of smoothing determined by dose-response curves and the Akaike's Information Criteria (AIC)	Temperature, humidity, time, day of the week, holidays, unusual events such as thunderstorms, influenza	> Association between cardiac admissions and PM_{10}, NO_2 and SO_2 in both cities	>Generally consistent results between the two cities however authors reported a positive association between O_3 and cardiac admissions in Hong Kong, negative in London > Single and 2-pollutant results reported

Table 1.2 Summary of recent short-term gaseous pollutant and hospital admission studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Burnett et al. (1999) >Toronto, Ontario >1980 to 1994 (66)4)	Heart failure, IHD, cerebrovascular diseases, diseases of peripheral circulation	$PM_{2.5}$, $PM_{10-2.5}$, PM_{10}, NO_2, SO_2, O_3 (0-2)	Time-series, Forward-stepwise regression, best model chosen based on AIC	Temperature, humidity, dew point, day of week, seasonal	> Association between all pollutants and cardiovascular outcomes except ozone and cerebrovascular diseases	> Study emphasized the importance of multi-pollutant models > Authors commented that single pollutant models may overestimate the effect of particulate matter and underestimate the effect of gaseous pollutants

Table 1.2 Summary of recent short-term gaseous pollutant and hospital admission studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Wong et al. (1999) >Hong Kong >1994 to 1995 (49)7)	All cardiovascular, heart failure, IHD, cerebrovascular admissions (population divided into age groups)	PM_{10}, NO_2, SO_2, O_3 (0-3)	Time-series, Poisson regression, best lag chosen based on AIC	Temperature, humidity, season	> Association between all pollutants and cardiovascular and heart failure admissions > Elderly had larger relative risks	> Multi-pollutant models were not investigated
Morgan et al. (1998) > Sydney, Australia > 1990 to 1994 (55)3)	Heart disease in those > 65 years of age	Particulates, NO_2, O_3 (0-2)	Time-series, Poisson regression with generalized estimating equations (GEE)	Temperature, day of week, dew point, holidays	> Association between heart disease and NO_2 and O_3 (single pollutant) > Association between heart disease and NO_2 (multi-pollutant)	> The number of monitoring stations varied from 3 to 14 over the study period

Table 1.2 Summary of recent short-term gaseous pollutant and hospital admission studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Burnett et al. (1997) > 10 largest Canadian cities > 1981 to 1991 (32)0)	Heart failure hospitalizations for those >= 65 years	Coefficient of haze, CO, NO_2, SO_2, O_3 (0-3)	Time-series, Poisson regression with GEE	Temperature, dew point, time, day of the week	> Association between heart failure and CO, NO_2, SO_2 and COH	> Estimates "vary considerably among cities" > Relative risk estimates for each month per city, estimate pooled for year
Pönka and Virtanen (1996) > Helsinki, Finland > 1987 to 1989 (51)9)	Ischemic heart disease and cerebrovascular disease	Total suspended particles, NO, NO_2, SO_2, O_3 (0-7)	Time-series, Poisson regression	Temperature, humidity, trends, seasonal, day of the week, cold weather, influenza	> Association between IHD ER admissions and NO and O_3 > Association between cerebrovascular admissions and NO_2	> Emergency and hospital admissions were studied separately

Table 1.2 Summary of recent short-term gaseous pollutant and hospital admission studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Schwartz and Morris. (1995) > Detroit, Michigan > 1986 to 1989 (41)9)	Ischemic heart disease and heart failure admissions for those aged 65 years and older	PM_{10}, CO, SO_2, O_3 (0-2)	Time-series, Poisson regression, autoregression	Temperature, dew point temperature, time, month of study, day of the week, warm/cool season	> PM_{10} and CO were significantly associated with heart failure > O_3 was not associated with any outcome > PM_{10} significant predictor of ischemic heart disease admissions	> Pollutant levels were markedly higher in Detroit compared to Vancouver > Detroit IHD and heart failure mean admissions were more than double the daily averages in Vancouver
Morris et al. (1995) > 7 US cities > 1986 to 1989 (45)3)	Heart failure amoung elderly	CO, NO_2, SO_2, O_3 (0-7)	Time-series, Generalize linear models with LOESS smoothing	Temperature, weather, seasonal effects, weekly cycles	> Significant association between heart failure and CO in all 7 cities	> Admissions increased monotonically with CO > Models without lags showed the strongest association > Age of 'elderly' was not defined

Table 1.3 Summary of recent short-term gaseous pollutant and mortality studies

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Burnett et al. (2004) >12 Canadian cities > 1981 to 1999 (67)5)	Cardiovascular mortality	$PM_{2.5}$, PM_{10}, CO, NO_2, SO_2, O_3, (0-2)	Time-series, spline smoothing with AIC	Humidex, season, time	> Association between 3 day moving average of NO_2 and cardio mortality	> Reported pooled estimates across the 12 cities > Individual city results varied, cardio mortality city specific results not reported
Kan et al. (2003) > Shanghai, China > 1991 to 1999 (54)2)	Stroke mortality	PM_{10}, NO_2, SO_2	Time-series, Generalized additive model, nonparametric smoothing with AIC	Temperature, humidity, dew point day of the week, season, time	> Association between NO2 and stroke (single pollutant model) > Multiple pollutant models were not significant	> Reported results with pollutant lagged 1 day

Table 1.3 Summary of recent short-term gaseous pollutant and mortality studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Wong et al. (2002) > Hong Kong > 1995 to 1998 (48)6)	Cardiovascular, IHD and cerebrovascular mortality	PM_{10}, NO_2, SO_2, O_3 (0-7)	Time-series, Poisson regression, best lag period chosen based on AIC	Temperature, humidity, seasonal, day of week	> Association between IHD mortality and all 4 pollutants (single pollutant models) > NO_2 associated with IHD when adjusted for other pollutants	> Hong Kong had almost double the mean deaths per day than Vancouver > Single-pollutant model results were reported across different lag periods
Hong et al. (2002) > Seoul, Korea > 1991 to 1997 (53)1)	Ischemic and hemorrhagic stroke mortality	TSP, CO, NO_2, SO_2, O_3 (0-4)	Time-series, Generalized additive model, LOESS, AIC	Temperature, relative humidity, season, time, day of the week, atmospheric pressure	> Association between pollutants and ischemic stroke	> Reported single and 2-pollutant model results but no multiple pollutant models > Authors suggest O_3 has a threshold of ~25 ppb

Table 1.3 Summary of recent short-term gaseous pollutant and mortality studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Hong et al. (2002) > Seoul, Korea > 1995 to 1998 (52)0)	Stroke deaths	PM_{10}, CO, NO_2, SO_2, O_3 (0-5)	Time-series, Generalized additive model, LOESS, AIC	Temperature, humidity, barometric pressure, season, time, day of the week	> Strongest association between stroke and same day O_3, but NO_2, SO_2 and CO in the 2-day lag model	> Reported single and 2-pollutant model results but no multiple pollutant models
Goldberg et al. (2002) > Montreal, Quebec > 1984 to 1993 (68)6)	Heart failure 1 year before death, heart failure deaths year-round and by warm/cool season	Coefficient of haze, CO, NO_2, SO_2, O_3 (0-5)	Time-series, Generalized linear Poisson model, natural splines, AIC	Temperature, humidity, barometric pressure, season, trend, day of week	> Association between heart failure 1 year before death and SO_2 and NO_2	> Defined heart failure 1 year before death population based on health services rendered and filled prescriptions
Goldberg et al. (2001) > Montreal, Quebec > 1984 to 1993 (69)7)	Cardiovascular (population divided into < 65 years and >= 65 years) year-round and by warm/cool season	O_3 (0-5 and 3 day mean)	Time-series, Generalized additive model, LOESS, AIC	Weather, season, trend	> Association between cardiovascular and 3-day mean O_3 > Association between cardiovascular in those >= 65 and 3-day mean O_3	> Reported single pollutant model results

Table 1.3 Summary of recent short-term gaseous pollutant and mortality studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Hoek et al. (2001) > Netherlands > 1986 to 1994 (47, 70)8)	Specific cardiovascular deaths including IHD and heart failure	PM_{10}, CO, NO_2, SO_2, O_3	Time-series, Poisson regression with generalized additive models	Temperature, humidity, day of the week, seasonal, influenza epidemics and holidays	> Association between CO, NO_2, SO_2, and O_3 and all-cause and heart failure mortality	> Reported single-pollutant models results > No lag periods
Hong et al. (1999) > Inchon, South Korea > Jan 1995 to Aug 1996 (71)9)	All-cause and cardiovascular deaths	PM_{10}, CO, NO_2, SO_2, O_3 (0-6)	Time-series, Generalized additive models	Temperature, humidity, time, season	> Results concentrated on PM_{10} > Negative relationship between ozone and daily mortality	> 20-month study period > Created an index to evaluate combined effects of pollutants > Authors suggest that the negative relationship was due to low levels of O_3 (15.4 ppb)

Table 1.3 Summary of recent short-term gaseous pollutant and mortality studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Burnett RT et al. (1998) > 11 Canadian cities > 1980 to 1990 (35)3)	Non-accidental deaths	CO, NO_2, SO_2, O_3	Time-series, Generalize additive model, summary estimates calculated by averaging city-specific risks	Temperature, humidity, dew point temperature, trends, seasonal, sub seasonal (short-term epidemics) day of the week	> All pollutants had an association with non-accidental death (averaged across the 11 cities) > NO_2 had the largest effect on mortality, followed by O_3, SO_2 and CO	> Pollutant contributions to the overall risk of death was different in each city; for Vancouver the % increased risk of death attributable to CO was 0.00, NO_2 was 7.2, SO_2 was –0.3 and O_3 was1.4 > Data sources were not reported
Zmirou et al. (1998) > 10 large European cities > 1977 to 1990 (inconsistent across cities) (72)0)	Cardiovascular disease year-round and by warm/cool season	TSP, black smoke, NO_2, SO_2, O_3 (0-3)	Poisson meta-analysis	Temperature, humidity, day of the week, holidays, season	> SO_2 and O_3 associated with cardiovascular mortality (pooled estimated)	> Different time periods in each city > Multiple pollutant results referred to but not reported > Different number of monitoring stations in each city > Different covariates in each city

Table 1.3 Summary of recent short-term gaseous pollutant and mortality studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Morgan et al. (1998) > Sydney, Australia > 1989 to 1993 (73)1)	All-cause and cardiovascular mortality	Particulates, NO_2, O_3 (0-2 and cumulative lags)	Time-series, Poisson regression with GEE	Temperature, dew point, day of week, season	> Gaseous pollutants not significantly associated with cardiovascular mortality	> Pollutants lagged at different periods in the multiple pollutant models > Number of monitoring stations varied during the study
Anderson et al. (1996) > Greater London > 1987 to 1992 (42)0)	Non- accidental all-cause, respiratory and cardiovascular deaths year-round and by warm/cool season	Black smoke, NO_2, SO_2, O_3 (0-3)	Time-series, Poisson auto regression	Temperature, humidity, day of week, seasonality, flu epidemic, holidays	> O_3 was significantly associated with all-cause, respiratory and cardiovascular mortality year-round and during the warm season > NO_2 was significantly associated with cardiovascular mortality in the warm season	> Pollutant measures were not taken for the complete day > O_3 concentrations were only measured from one monitoring station

Table 1.4 Summary of recent short-term gaseous pollutant and combined morbidity and mortality studies

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Anderson et al. (2001) > West Midlands conurbation, UK > Oct 1994 to Dec 1996 (74)2)	Cardiovascular deaths and hospitalizations including cardiac, ischemic heart disease and stroke	Black smoke, $PM_{2.5}$, $PM_{2.5\text{-}10}$, CO, NO_2, SO_2, O_3 (0-3)	Time-series, General additive model	Temperature, humidity, influenza epidemics, day of the week, time, season	> No strongly significant morbidity or mortality associations	> 27 month study period > Unexplained negative associations
Gwynn et al. (2000) > Buffalo, New York > May 1988 to Oct 1990 (75)3)	Cardiovascular deaths and hospitalizations	H^+, Black smoke, COH, PM_{10}, CO, NO_2, SO_2, O_3 (0-3)	Time-series, Log-linear models	Temperature, relative humidity, weather, days of the week, time, season	> No pollutant strongly associated with cardiovascular hospitalizations > PM_{10} associated with cardiovascular deaths	> Single pollutant models > Different weather adjustments for models > Reported results for most significant lag period

Table 1.4 Summary of recent short-term gaseous pollutant and combined morbidity and mortality studies (continued)

Study	Cardiovascular outcome of interest	Pollutants studied (With lag period)	Model/analysis	Other covariates considered	Significant cardiovascular and gaseous pollutant conclusions	Comments
Prescott et al. (1998) > Edinburgh, UK > Jan 1981 to Jun 1995 and Oct 1992 to Jun 1995 (76)4)	Cardiovascular deaths and hospitalizations	Black smoke, PM_{10}, CO, NO_2, SO_2, O_3, (0-3)	Time-series, Poisson log linear regression	Temperature, wind speed day of week, time, season	> Negative significant association between O_3 and cardiovascular hospitalizations for those >= 65 years of age	> NO_2, O_3, CO, PM_{10} only available for the shorter study period

1.5.3. Potential mechanisms

Heart rate variability

The mechanism by which gaseous air pollution influences cardiovascular conditions is unclear. A study examining air pollution and the incidence of cardiac arrhythmia in a sample of 100 cardiac patients with implanted defibrillators found that NO_2 was associated with arrhythmia when NO_2 was lagged 1-day or across a 5-day moving average. However, CO, SO_2 and O_3 were also studied and did not show a strong or consistent association.(77) Another study involving patients with coronary heart disease and patients with more than one major coronary heart disease risk factor reported that environmental exposure to NO_2 was associated with reducing heart rate variability, noting that the main effect of NO_2 on reducing heart rate variability occurred within eight hours of exposure. Similar associations were not found for other gaseous pollutants.(37) One study conducted with 21 elderly participants did not find an association between heart rate variability and CO, NO_2 or SO_2 but did observe increased heart rates and decreased heart rate variability with particulates and ozone.(78) Conversely, a recent population-based cross-sectional study found that elevated levels of air pollution, including CO, NO_2 and SO_2 were associated with increased heart rates and a decrease in heart rate variability. Considering the association between increased heart rate, a decrease in heart rate variability and the development of cardiovascular conditions, the results of the study led the authors to suggest an elevated level of air pollution increases the risk of cardiovascular conditions.(79)

Respiratory link

There have been suggestions that air pollution aggravates existing cardiovascular conditions through respiratory mechanisms. Air pollutants may decrease the ability of the lungs to oxygenate the blood or the ability of the blood to deliver oxygen leading to hypoxia, a deficiency of oxygen reaching the tissues of the body.(16) This condition could result in an increased demand on the heart muscle leading to myocardial infarction or heart failure.(41, 45) One study specific to ozone reported that exposure to ozone for four hours increased baseline values of total vascular resistance in directly exposed pulmonary vessels.(56)

Other (plasma viscosity, vasoconstriction, etc.)

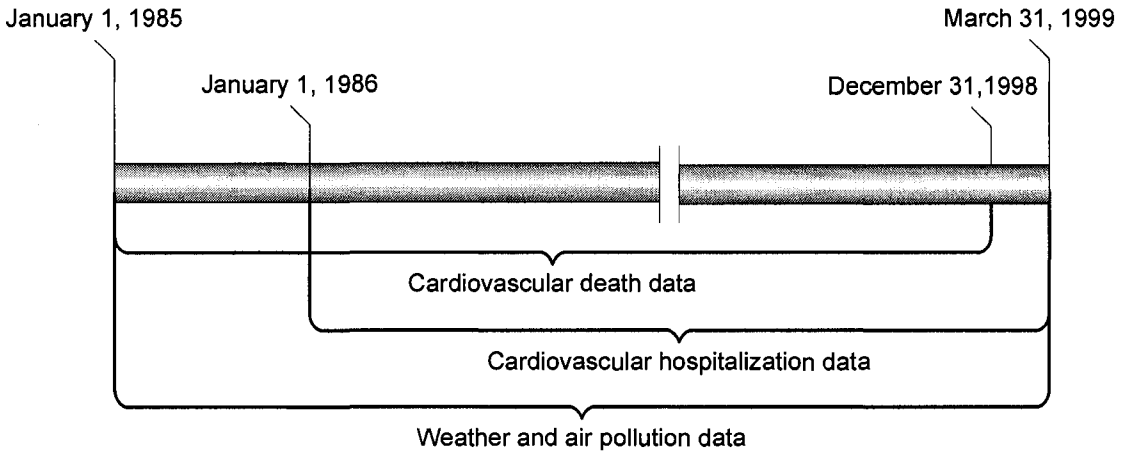
Several other studies have speculated about the mechanism by which air pollution influences cardiovascular conditions. Peters et al. reported an association between air pollution and increased plasma viscosity.(80) Brook et al. reported that short-term exposure to a mix of fine particulate and ozone at levels observed in urban environment induced artery vasoconstriction in healthy adults, however the effect of ozone alone was not reviewed.(81) There has also been a less probable suggestion that there exists some component of air pollutants that have a toxic effect on the heart.(45) Specifically for stroke, Hong et al. suggested that "...free radicals produced by air pollutants may cause inflammatory responses and enhanced blood coagulation and plasma viscosity..." which would in turn add to the risk of ischemic stroke.(53)

2. CHAPTER 2 MATERIALS AND METHODS

2.1. Study location and period

The analysis for this study was based on daily air pollution, hospitalization and mortality data from the Greater Vancouver area. Mortality data were available for January 1, 1985 to December 31, 1998 and hospitalization data were available for the time period between January 1, 1986 and March 31, 1999. Weather and air pollution data were available for the time covering both the hospitalization and death study periods; January 1, 1985 to March 31, 1999.

Figure 2.1 Study period



2.2. Hospitalization and mortality data

For this study, hospital admission and mortality data from 13 census subdivisions in the Vancouver area were obtained from the British Columbia Linked Health Dataset. The BC database uses probabilistic linkage theory and a linkage-coordinating file to link individuals' various health records from the province's health insurance program. The

BC Linked Health Dataset is composed of six types of health files including hospital separations, medical services, drug prescriptions for the elderly, long term care services, death and birth data. The BC dataset covers virtually all residents of British Columbia.(9, 82) Chamberlayne et al. has previously published a further description of the dataset.(83)

International Classification of Disease, Ninth Revision (ICD9) diagnostic codes were used to identify cardiovascular hospital admissions and deaths. The cardiovascular conditions under investigation were the more pervasive conditions according to the Heart and Stroke Foundation of Canada; stroke (ICD9 430-432, 434, 436), ischemic heart disease (ICD9 410-414), acute myocardial infarction (ICD9 410) and heart failure (ICD9 428), along with all cardiovascular conditions (ICD9 390-459).(2)

For this study, hospitalizations that met all of the following conditions were extracted from the BC Linked Heath Dataset:

- Cardiovascular condition specified in one of the first five diagnoses of the hospital discharge record;
- Admitted under the urgent or emergent admission type;
- Aged 65 years and older;
- Greater Vancouver resident.

The hospitalization dataset was restricted to those admitted under the urgent or emergent admission types to ensure that planned hospital visits and transfers from other facilities were excluded. The age group of 65 years and older was selected because

age is a central risk factor for heart diseases and stroke and older age groups have the highest rates of cardiovascular disease.(2, 20, 25)

The underlying cause of death and place of death information from death certificates in the BC linked dataset was used to determine the cardiovascular death counts. The underlying cause of death was coded according to ICD9, similar to diagnoses on hospital discharge records, and place of death was used to exclude deaths outside of Greater Vancouver from the analysis. Table 2.1 shows the crude counts of cardiovascular hospitalizations and deaths for the study period between 1985 and 1999 for the elderly living in Vancouver.

Table 2.1 Summary counts of cardiovascular hospitalizations and deaths for the elderly living in Vancouver, Canada

	Hospitalization (January 1, 1986 – March 31, 1999)	**Death** (January 1, 1985 – March 31, 1999)
All cardiovascular conditions	228,014	55,675
Stroke	22,995	11,136
Ischemic heart disease	103,050	29,620
Acute myocardial infarction	23,042	16,060
Heart failure	59,752	3,285

2.3. Environmental data

Daily weather and pollutant data were available for the complete study period from January 1, 1985 to March 31, 1999. Five to 31 monitoring stations measured gaseous air pollutant levels within Greater Vancouver on a daily basis. Daily levels of CO (six stations), SO_2 (four stations) and NO_2 (30 stations) were available while daily levels of the maximum one-hour O_3 concentration were available from 25 stations. Pollutant

concentrations measured from the multiple stations were averaged to determine an overall pollutant level for Greater Vancouver. Weather condition information was captured daily from a monitoring station at the Vancouver International Airport.(9) Weather information included daily average temperature and daily average dew point temperature. Complete pollution data were available while weather data were available for over 99% of the 5,203 study days. Missing data were acquired from the online Environment Canada climate archives.(84)

Chemical reactions that form ozone are influenced by temperature and sunlight, therefore, seasonal analysis was completed with ozone in relation to each cardiovascular condition.(28) The seasons were defined as warm (April to September) and cool (October to March) based on other studies that have conducted similar warm/cool seasonal analyses with ozone.(42, 68, 69, 85)

2.4. Methodology

Published studies have incorporated a variety of modeling methods and there are varying views on what constitutes the 'best' time-series model for air pollution investigations. Given the different published modeling techniques, this project utilized the methodology of the widely cited National Morbidity, Mortality and Air Pollution Study (NMMAPS) conducted at the Johns Hopkins University.(86-88)

The NMMAPS generalized linear model was used to determine if there was a relationship between air pollution and cardiovascular mortality and morbidity. Several smooth functions (natural cubic splines) were included in the model to control for the potential confounding effects of time, weather conditions and day of the week. Splines

divide a continuous variable into a set of discrete ranges. The end points of the ranges are referred to as knots. A separate regression polynomial is then fit within each range. When modelling with spline functions one can specify degrees of freedom instead of knots. Each knot uses one degree of freedom. The selection of degrees of freedom is an important part of time-series analysis. Degrees of freedom must be selected that are large enough to remove the effect of confounding factors but not too large that the air pollution effects are eliminated. Fewer knots represent smoother fits while n knots (where n is the sample size) would be equivalent to no smoothing.(89, 90)

Seven degrees of freedom per year allowed information within a short time period (approximately two months) to be utilized to estimate the logarithmic relative risks of mortality and morbidity of each cardiovascular condition. Natural cubic splines were also used to model smooth functions of temperature and dew point temperature to control for the effects of weather and humidity on the outcome (mortality/morbidity). The same day's temperature and the average temperature from the previous three days were each modeled with six degrees of freedom. Similar functions with dew point temperature were modeled with three degrees of freedom. Finally, to allow for different baseline hospitalization and death rates on different days of the week, a day of the week indicator variable was included in the model.(86)

The following equation represents the model utilized to estimate the relative increase in the logarithmic number of daily deaths and hospitalizations per unit increase in the concentration of each pollutant.

$$\text{Log}(E(Y)) = \beta X_i + \text{DOW} + S_1(\text{time}, 7\text{df/year}) + S_2(\text{temp}_0, 6\text{df}) + S_3(\text{temp}_{1\text{-}3}, 6\text{df}) + S_4(\text{dew}_0, 3\text{df}) + S_5(\text{dew}_{1\text{-}3}, 3\text{df})$$

Where:

Y is the count of cardiovascular deaths/hospitalizations on a given day

E (Y) is the expected value of Y on the given day

β is the log-relative rate of morbidity/morality associated with a one unit increase in pollution variable X_i

X_i is the air pollution level

DOW is a set of 6 indicator variables for the days of the week

S_1 (time, 7df/year) is the smooth function of time

S_2 (temp_0, 6df) is the smooth function of same day's temperature

S_3 ($\text{temp}_{1\text{-}3}$, 6df) is the smooth function of the average temperature of the previous three days

S_4 (dew_0, 3df) is the smooth function of same day's dew point temperature

S_5 ($\text{dew}_{1\text{-}3}$, 3df) is the smooth function of the average dew point temperature of the previous three days

Using the estimates from the above model, the percentage of change in the mean number of daily hospitalizations and deaths was calculated based on the increase in exposure corresponding to the interquartile range (between the 25th and 75th percentiles

of the distribution of the pollutant concentrations) of each air pollutant. This allows comparisons between different pollutants and comparisons that are not affected by the different measurement units and baseline concentrations. Additionally, under the assumption that the estimated regression coefficient was normally distributed, the upper and lower 95 percent confidence limits of the mean percentage of change were calculated.

Following the NMMAPS study, models using the pollutant concentrations of current day (no lag), previous day (lag 1 day) and the mean of the two lags were considered. Single pollutant models, models with all gaseous pollutants except ozone, and models with all gaseous pollutants were all reviewed. Additionally, warm and cool seasonal models were considered to investigate the relationship between ground-level ozone and each cardiovascular disease. All analyses were completed using statistical software SAS system for windows (release 8.2) and S-Plus 6.0 Professional Edition for Windows (July 2001).

3. CHAPTER 3 RESULTS

3.1. Summary statistics of gaseous air pollution, weather conditions and cardiovascular hospitalizations and deaths

Table 3.1 provides summary statistics of gaseous air pollution, weather conditions and cardiovascular hospitalizations and deaths. During the study period concentrations of gaseous air pollutants were low. Maximum levels of CO, NO_2 and SO_2 were well below the Canadian National Ambient Air Quality Objectives maximum acceptable levels (CO: 43% of the NAAQO; NO_2: 44%; and SO_2: 27%). Ozone was below the maximum acceptable level (82 ppb) on over 99% of the 5,203 study days.

There were 228, 014 cardiovascular hospitalizations between January 1, 1986 and March 31, 1999, with an average of approximately 47 per day. There were fewer cardiovascular deaths (55,675) during the study period, with an average of only about 11 per day. On average, about half of the cardiovascular hospitalizations had ischemic heart disease specified as a diagnostic condition. There were about 12 heart failure hospitalizations per day and there were similar numbers of AMI and stroke hospitalizations during the study period. For cardiovascular deaths, deaths were more frequently due to ischemic heart disease than to any of the other cardiovascular conditions under investigation. On average there was less than one death per day due to heart failure between January 1, 1985 and December 31, 1998.

Table 3.1 Distribution of daily levels of gaseous air pollution, daily weather conditions, daily cardiovascular hospitalizations and daily cardiovascular deaths for elderly in Vancouver, Canada

Variable	Mean	SD	Min	Percentiles			Max	IQR
				25^{th}	50^{th}	75^{th}		
Gaseous air pollution								
Average CO (ppm)	1.01	0.60	0.20	0.62	0.83	1.18	5.58	0.56
Average NO_2 (ppb)	19.34	6.29	4.28	15.06	18.11	22.18	70.00	7.12
Average SO_2 (ppb)	4.85	3.00	0.00	2.75	4.25	6.25	30.50	3.50
Maximum 1-hr O_3 (ppb)	27.95	11.81	1.27	19.85	27.67	35.24	105.50	15.39
Weather								
Daily average temperature (°C)	10.38	5.89	-11.50	6.10	10.20	15.40	25.90	9.30
Daily average dew point temperature (°C)	6.70	5.41	-25.60	3.30	7.10	11.00	19.00	7.70
Cardiovascular hospitalizations								
All cardiovascular (n=228,014)	47.13	11.3	4	39	46	55	89	16
Stroke (n=22,995)	4.75	2.32	0	3	5	6	15	3
IHD (n=103,050)	21.30	5.58	2	17	21	25	41	8
AMI (n=23,042)	4.76	2.30	0	3	5	6	16	3
Heart failure (n=59,752)	12.35	4.52	0	9	12	15	31	6
Cardiovascular deaths								
All cardiovascular (n=55,675)	10.90	3.93	0	8	11	13	25	5
Stroke (n=11,136)	2.18	1.56	0	1	2	3	9	2
IHD (n=29,620)	5.80	2.65	0	4	6	7	16	3
AMI (n=16,060)	3.13	1.84	0	2	3	4	12	2
Heart failure (n=3,285)	0.64	0.83	0	0	0	1	6	1

Table 3.2 shows the Pearson correlation coefficients between the gaseous air pollutants utilized during the study. With an exception of ozone, the gaseous pollutants were positively correlated with each other. The strongest positive correlation can be seen between CO and NO_2 with a Pearson correlation coefficient of 0.72. All the correlations were highly significant. The p-value of the correlation between NO_2 and O_3 was about 0.01 and the other p-values were all less than 0.001.

Table 3.2 Pearson correlation coefficients between daily concentrations of gaseous air pollutants in Vancouver, Canada

Gaseous air pollutant	**CO**	**NO_2**	**SO_2**	**O_3**
CO	1.00	0.72	0.64	-0.38
NO_2		1.00	0.61	-0.03
SO_2			1.00	-0.14
O_3				1.00

Table 3.3 shows that average temperature and average dew point temperature were highly correlated (r = 0.94). Correlations between weather conditions and air pollutants are shown in Table 3.4. CO, NO_2 and SO_2 were negatively correlated with both average temperature and average dew point temperature whereas O_3 was positively correlated with both weather variables. The p-value of all correlations presented in Tables 3.3 and 3.4 were less than 0.001.

Table 3.3 Pearson correlation coefficients between daily weather conditions in Vancouver, Canada

Weather condition	Average temperature	Average dew point temperature
Average temperature	1.00	0.94
Average dew point temperature		1.00

Table 3.4 Pearson correlation coefficients between daily concentrations of gaseous air pollutants and weather conditions in Vancouver, Canada

Gaseous air pollutant	CO	NO_2	SO_2	O_3
Average temperature	-0.40	-0.26	-0.10	0.53
Average dew point temperature	-0.32	-0.23	-0.06	0.35

3.2. Temporal trends in gaseous air pollution, weather conditions and cardiovascular hospitalizations and deaths

Summary statistics by season are shown in Table 3.5 and Figures 3.1, 3.2 and 3.3 for the air pollution, weather, cardiovascular hospitalization and cardiovascular death variables under investigation. The seasons were defined by month; spring (March to May), summer (June to August), fall (September to November) and winter (December to February). On average, levels of CO, NO_2 and SO_2 were higher in the winter compared to the spring and summer. For all cardiovascular conditions including the specific conditions under investigation, on average there were more hospitalizations and deaths in the winter months compared to other seasons. By contrast, ozone levels, along with the weather variables, were higher in the summer, on average, compared to the fall and winter seasons.

Table 3.5 Mean (standard deviation) of daily levels of gaseous air pollution, daily weather conditions, daily cardiovascular hospitalizations and daily cardiovascular deaths in the elderly by season in Vancouver, Canada

Variable	Spring	Summer	Fall	Winter
Gaseous air pollution				
Average CO (ppm)	0.82 (0.32)	0.71 (0.25)	1.11 (0.56)	**1.37 (0.83)**
Average NO_2 (ppb)	18.83 (5.75)	16.91 (5.53)	19.92 (6.34)	**21.63 (6.54)**
Average SO_2 (ppb)	4.07 (2.20)	4.46 (2.20)	5.42 (3.33)	**5.45 (3.65)**
Maximum 1-hr O_3 (ppb)	34.48 (7.99)	**34.58 (12.34)**	23.21 (9.51)	19.55 (8.51)
Weather				
Daily average temperature (°C)	9.83 (3.43)	**17.24 (2.24)**	10.60 (4.63)	4.05 (3.62)
Daily average dew point temperature (°C)	5.72 (3.49)	**12.16 (2.14)**	7.52 (4.63)	1.59 (4.60)
Cardiovascular hospitalizations				
All cardiovascular	47.94 (11.59)	44.26 (10.53)	46.70 (10.54)	**49.53 (11.79)**
Stroke	4.71 (2.26)	4.53 (2.27)	4.80 (2.37)	**4.97 (2.36)**
IHD	21.86 (5.80)	20.14 (5.38)	21.13 (5.31)	**22.03 (5.59)**
AMI	4.87 (2.25)	4.45 (2.24)	4.85 (2.32)	**4.88 (2.36)**
Heart failure	12.90 (4.72)	10.98 (4.10)	12.03 (4.00)	**13.44 (4.81)**
Cardiovascular deaths				
All cardiovascular	11.09 (4.04)	9.88 (3.59)	10.75 (3.54)	**11.91 (4.24)**
Stroke	2.18 (1.60)	1.99 (1.48)	2.13 (1.50)	**2.42 (1.63)**
IHD	5.95 (2.73)	5.23 (2.45)	5.69 (2.43)	**6.34 (2.86)**
AMI	3.23 (1.89)	2.80 (1.72)	3.15 (1.78)	**3.37 (1.91)**
Heart failure	0.67 (0.85)	0.59 (0.79)	0.58 (0.78)	**0.72 (0.89)**

Note:
Larger mean values are shown in bold.

Figure 3.1 Mean daily concentration of gaseous air pollution by season in Vancouver, Canada

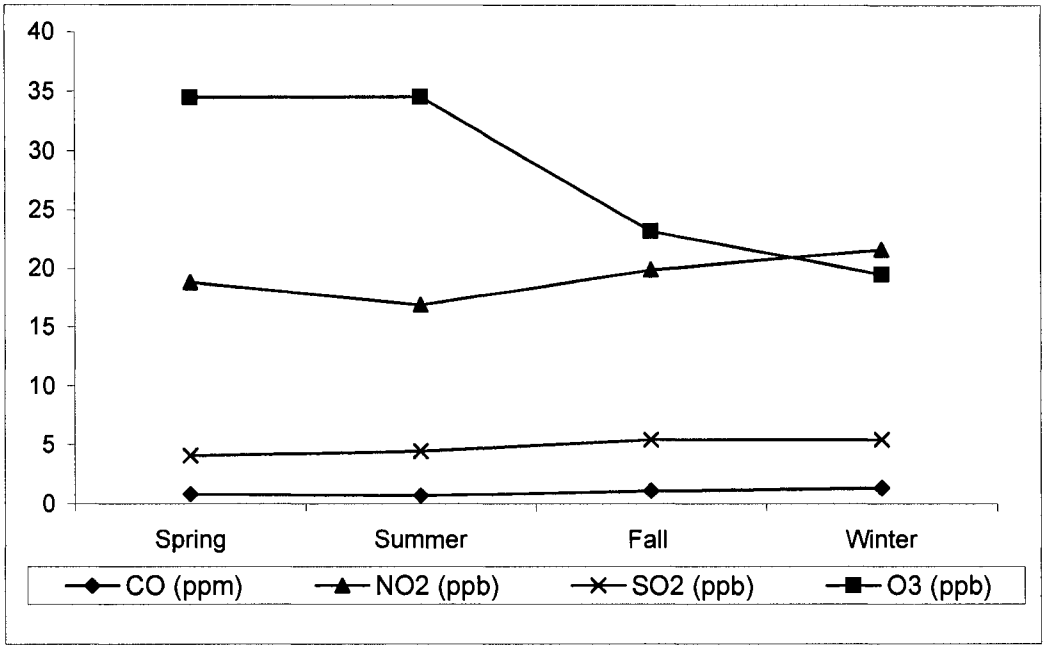


Figure 3.2 Mean daily cardiovascular hospitalizations in the elderly by season in Vancouver, Canada

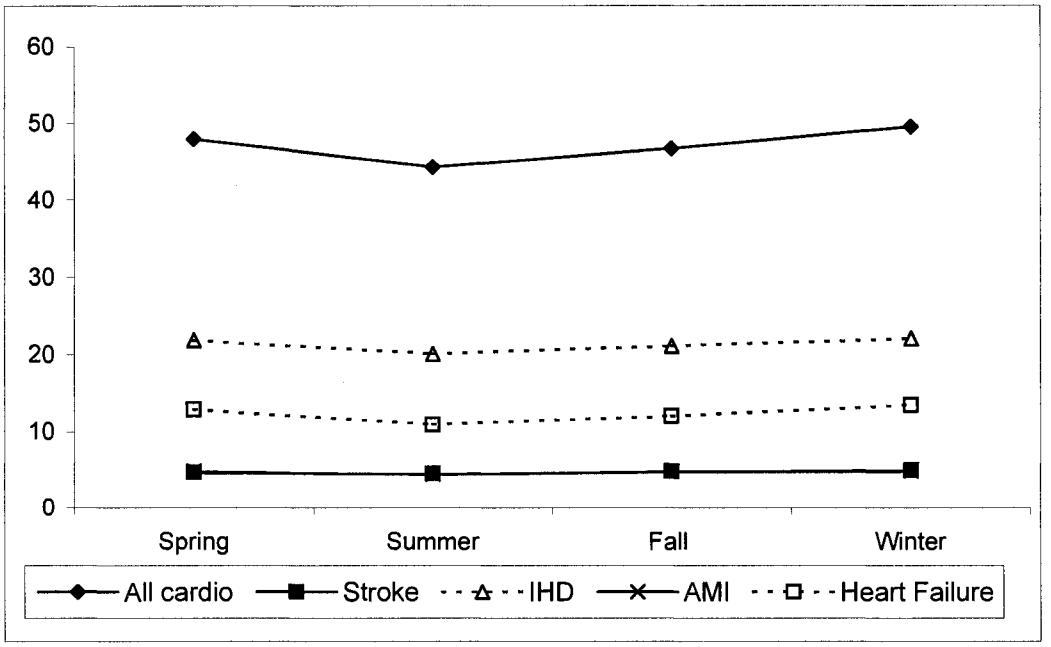
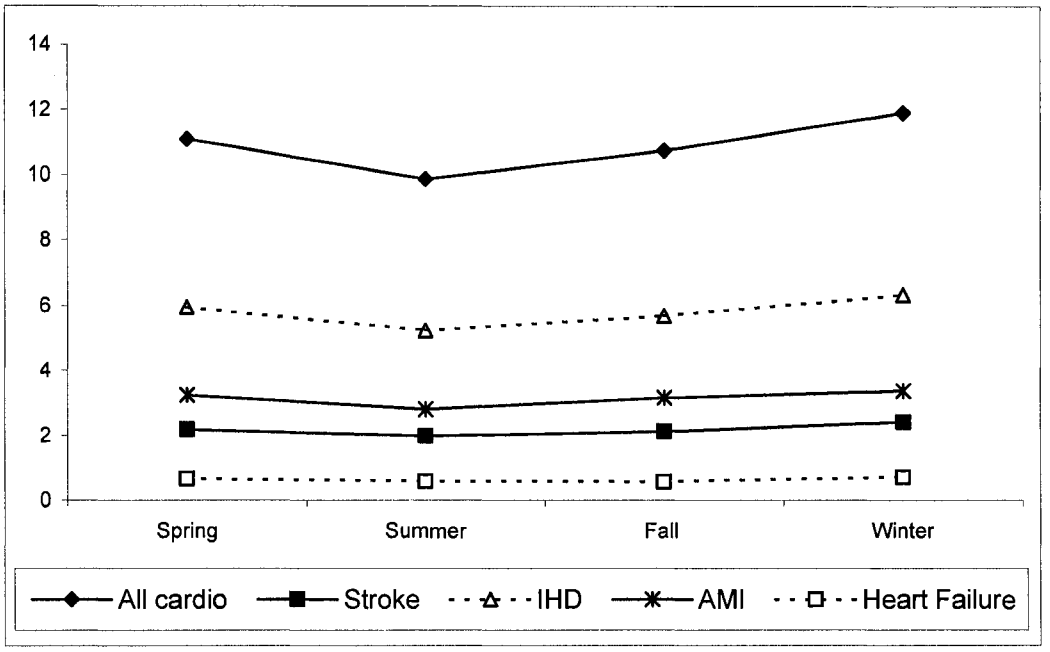


Figure 3.3 Mean daily cardiovascular deaths in the elderly by season in Vancouver, Canada



Air pollution, weather and cardiovascular hospitalization and death summary information by day of the week is shown in Table 3.6 and Figures 3.4, 3.5 and 3.6. The levels of air pollution were slightly higher during the weekdays with the exception of ozone. Temperature variables appeared to be consistent across the days of the week. With the exception of AMI, cardiovascular hospitalizations appeared to be more frequent on weekdays compared to weekends. Cardiovascular deaths did not show a consistent pattern by day of the week.

Table 3.6 Mean (standard deviation) of daily levels of gaseous air pollution, daily weather conditions, daily cardiovascular hospitalizations and daily cardiovascular deaths in the elderly by day of the week in Vancouver, Canada

Variable	Sun	Mon	Tue	Wed	Thurs	Fri	Sat
Gaseous air pollution							
Average CO (ppm)	0.84 (0.44)	0.97 (0.55)	1.04 (0.59)	1.09 (0.68)	1.09 (0.67)	**1.10 (0.65)**	0.93 (0.53)
Average NO_2 (ppb)	16.61 (5.31)	19.08 (5.97)	20.08 (6.31)	**20.59 (6.75)**	20.49 (6.48)	20.37 (6.29)	18.12 (5.75)
Average SO_2 (ppb)	4.22 (2.44)	4.65 (2.95)	4.88 (3.01)	5.23 (3.17)	**5.28 (3.16)**	5.10 (3.17)	4.59 (2.89)
Maximum 1-hr O_3 (ppb)	**29.43 (12.22)**	27.39 (11.09)	27.59 (11.54)	27.47 (11.59)	27.67 (11.89)	27.24 (11.64)	28.86 (12.50)
Weather							
Daily average temperature (°C)	10.36 (5.83)	10.36 (5.85)	10.39 (5.92)	10.39 (5.90)	**10.49 (5.90)**	10.42 (5.91)	10.30 (5.96)
Daily average dew point temperature (°C)	6.71 (5.29)	6.73 (5.47)	6.69 (5.41)	**6.77 (5.38)**	**6.77 (5.44)**	6.64 (5.53)	6.63 (5.35)
Cardiovascular hospitalizations							
All cardiovascular	39.54 (9.11)	**52.44 (11.12)**	51.25 (11.10)	49.67 (9.75)	49.59 (10.67)	48.82 (9.43)	38.60 (8.74)
Stroke	4.39 (2.27)	**5.07 (2.45)**	4.85 (2.32)	4.99 (2.38)	4.87 (2.24)	4.91 (2.29)	4.19 (2.14)
IHD	18.49 (4.85)	**23.52 (5.42)**	23.18 (5.78)	22.43 (4.99)	22.38 (5.24)	21.71 (4.88)	17.4 (4.61)
AMI	4.37 (2.19)	5.03 (2.29)	4.93 (2.47)	4.86 (2.22)	**5.04 (2.42)**	4.83 (2.23)	4.29 (2.16)
Heart failure	10.51 (3.96	**13.70 (4.83)**	13.09 (4.43)	12.63 (4.33)	12.62 (4.65)	13.02 (4.30)	10.89 (4.19)
Cardiovascular deaths							
All cardiovascular	10.74 (3.92)	**11.08 (3.94)**	10.81 (3.77)	10.85 (3.99)	11.05 (4.05)	11.01 (4.00)	10.78 (3.84)
Stroke	2.13 (1.52)	2.15 (1.51)	2.13 (1.56)	2.17 (1.54)	2.22 (1.60)	**2.25 (1.58)**	2.21 (1.62)
IHD	5.67 (2.55)	**5.96 (2.77)**	5.72 (2.55)	5.85 (2.62)	5.87 (2.73)	5.85 (2.73)	5.69 (2.60)
AMI	3.09 (1.78)	3.20 (1.88)	3.00 (1.76)	**3.22 (1.91)**	3.17 (1.93)	3.17 (1.83)	3.09 (1.79)
Heart failure	**0.68 (0.85)**	0.63 (0.85)	0.64 (0.80)	0.65 (0.85)	0.62 (0.82)	0.65 (0.83)	0.63 (0.82)

Note:
Larger mean values are shown in bold.

Figure 3.4 Mean daily concentration of gaseous air pollution by day of the week in Vancouver, Canada

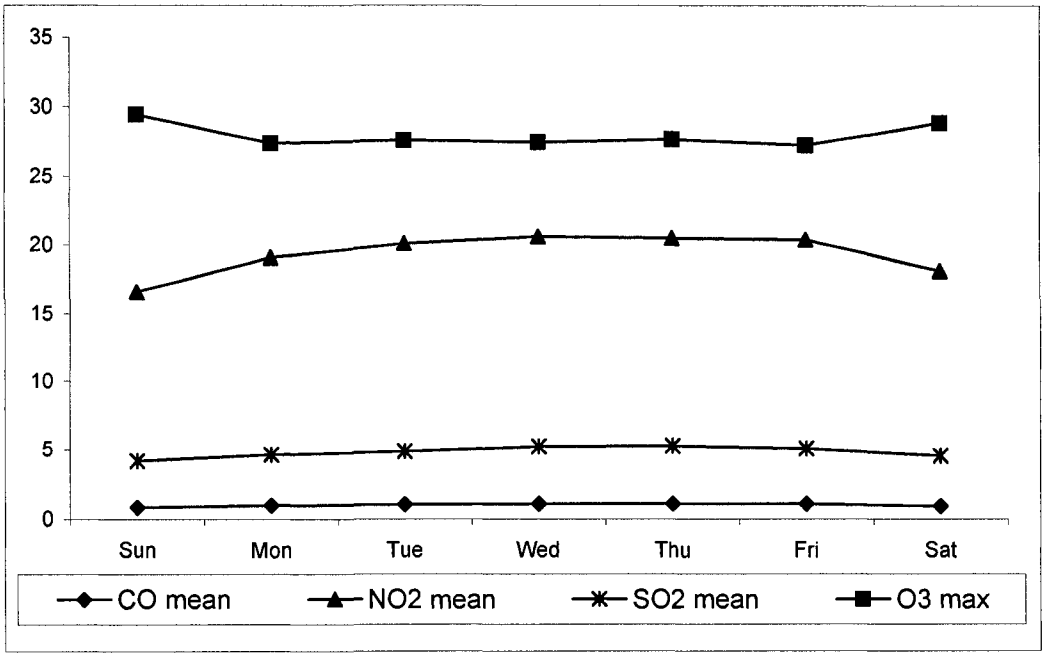


Figure 3.5 Mean daily cardiovascular hospitalizations in the elderly by day of the week in Vancouver, Canada

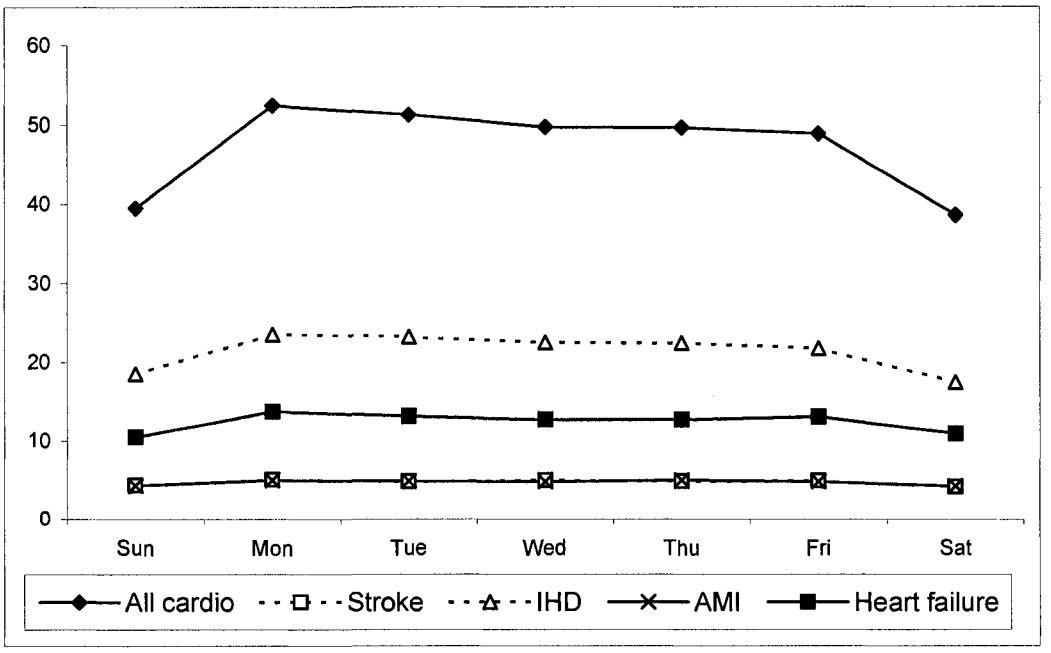


Figure 3.6 Mean daily cardiovascular deaths in the elderly by day of the week in Vancouver, Canada

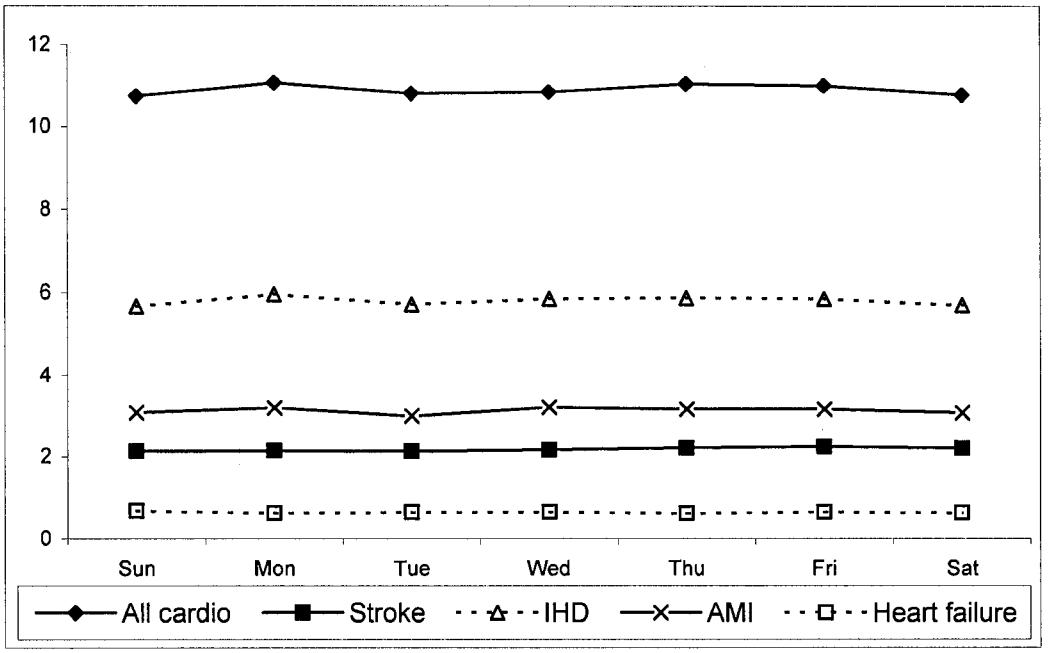


Table 3.7 shows summary information for the seasonal analysis. These seasons were divided into warm and cool with the cool season defined by the months of October to March and the warm season encompassed by the months of April to September. Levels of ozone and average temperature and dew point temperature were higher during the warm months, while cardiovascular hospitalizations and deaths were higher during the cool months.

Table 3.7 Mean (standard deviation) of daily levels of ozone, daily weather conditions, daily cardiovascular hospitalizations and daily cardiovascular deaths in the elderly by warm and cool season in Vancouver, Canada

Variable	Cool	Warm
Gaseous air pollution		
Maximum 1-hr ozone (ppb)	21.59 (8.73)	**24.51 (10.95)**
Weather		
Daily average temperature (°C)	5.94 (4.00)	**14.95 (3.57)**
Daily average dew point temperature (°C)	3.22 (4.71)	**10.29 (3.34)**
Cardiovascular hospitalizations		
All cardiovascular	**48.69 (11.48)**	45.51 (10.88)
Stroke	**4.89 (2.34)**	4.62 (2.29)
Ischemic heart disease	**21.83 (5.61)**	20.75 (5.49)
Acute myocardial infarction	**4.92 (2.35)**	4.60 (2.23)
Heart failure	**13.04 (4.61)**	11.64 (4.32)
Cardiovascular deaths		
All cardiovascular	**11.62 (4.08)**	10.19 (3.64)
Stroke	**2.33 (1.59)**	2.03 (1.51)
Ischemic heart disease	**6.18 (2.76)**	5.43 (2.48)
Acute myocardial infarction	**3.34 (1.90)**	2.93 (1.76)
Heart failure	**0.68 (0.86)**	0.61 (0.79)

Note:
Larger mean values are shown in bold.

3.3. Time-series results for pollutants in relation to daily cardiovascular hospitalizations and deaths

Time-series results are presented for each cardiovascular condition in association with each gaseous pollutant adjusted in three different models.

- Adjusted model A - pollutant and cardiovascular association adjusted for daily weather conditions;
- Adjusted model B - pollutant and cardiovascular association adjusted for daily weather conditions and other gaseous pollutants under investigation except ozone;
- Adjusted model C – pollutant and cardiovascular association adjusted for daily weather conditions and other gaseous pollutants under investigation (CO, NO_2, SO_2, and O_3).

All cardiovascular conditions

Table 3.8 shows the results of each gaseous pollutant in relation to daily cardiovascular hospitalizations. The results show a positive and statistically significant association of CO, NO_2, and SO_2 with daily cardiovascular hospitalizations for single pollutant models with no lag period and for models when the levels of pollutants were averaged between the same day and one previous day. The association remained statistically significant for CO and NO_2 when further adjusted for other pollutants CO, NO_2 and SO_2 in the same day pollutant models. The time-series model of same day levels of NO_2 in relation to all cardiovascular hospitalizations remained positive and statistically significant when adjusted for weather and all other gaseous pollutants (Mean percent change $_{no\ lag}$= 1.41 percent, 95 percent confidence interval (CI): 0.31, 2.51). Results for all ozone models

and all models with the pollutants lagged one day were non-significant. Table 3.9 presents the results of the time-series analysis for the pollutants in relations to cardiovascular deaths. Associations for all models were non-significant.

Table 3.8 Mean percentage of change in daily cardiovascular hospitalizations across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

All Cardiovascular Hospitalizations		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	CO	**1.71**	1.03	2.40	0.54	-0.13	1.23	**1.41**	0.64	2.17
Adjusted model B	CO	**1.15**	0.13	2.18	0.77	-0.25	1.80	1.17	-0.01	2.36
Adjusted model C	CO	1.01	-0.04	2.08	0.85	-0.21	1.92	1.14	-0.10	2.40
Adjusted model A	NO_2	**1.87**	1.13	2.62	-0.02	-0.76	0.71	**1.21**	0.37	2.06
Adjusted model B	NO_2	**1.25**	0.21	2.31	-0.97	-2.00	0.06	0.18	-1.03	1.40
Adjusted model C	NO_2	**1.41**	0.31	2.51	-1.06	-2.13	0.02	0.21	-1.08	1.51
Adjusted model A	SO_2	**0.99**	0.35	1.63	0.55	-0.10	1.20	**1.05**	0.30	1.80
Adjusted model B	SO_2	-0.34	-1.20	0.52	0.58	-0.29	1.47	0.18	-0.85	1.23
Adjusted model C	SO_2	-0.37	-1.22	0.49	0.60	-0.28	1.48	0.18	-0.86	1.22
Adjusted model A	O_3	-0.53	-1.49	0.45	-0.11	-1.02	0.81	-0.44	-1.57	0.70
Adjusted model C	O_3	-0.49	-1.52	0.55	0.27	-0.69	1.25	-0.08	-1.31	1.17

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3).
Statistically significant associations are shown in bold.

Figure 3.7 Mean percentage of change in daily cardiovascular hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions

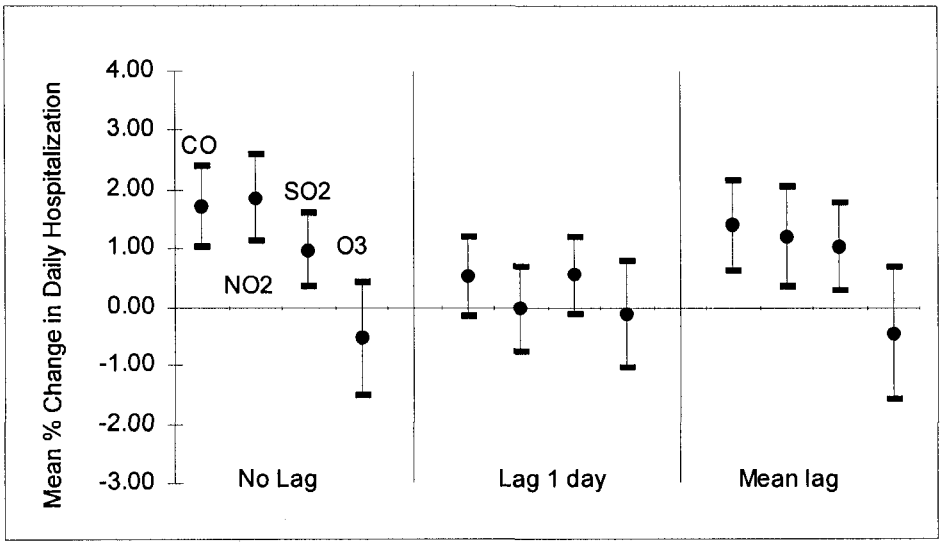


Figure 3.8 Mean percentage of change in daily cardiovascular hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions and gaseous pollutants (CO, SO_2, NO_2 and O_3)

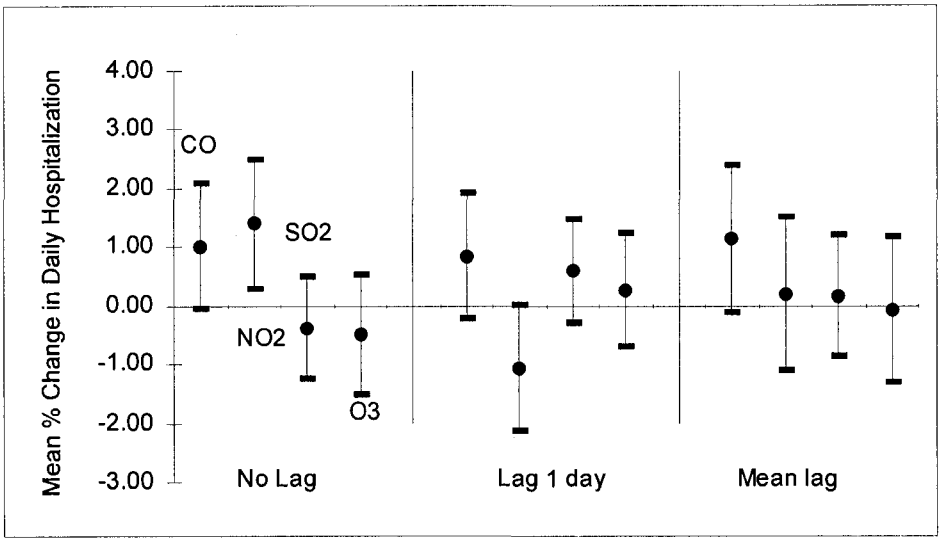


Table 3.9 Mean percentage of change in daily cardiovascular deaths across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

All Cardiovascular Deaths		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	CO	0.03	-1.24	1.32	0.33	-0.94	1.62	0.23	-1.20	1.67
Adjusted model B	CO	-0.79	-2.66	1.11	-0.48	-2.35	1.42	-0.89	-3.03	1.30
Adjusted model C	CO	-0.47	-2.40	1.51	-0.39	-2.32	1.59	-0.56	-2.82	1.74
Adjusted model A	NO_2	0.75	-0.67	2.18	1.13	-0.29	2.57	1.23	-0.39	2.87
Adjusted model B	NO_2	1.33	-0.66	3.35	1.71	-0.27	3.74	2.08	-0.25	4.46
Adjusted model C	NO_2	0.94	-1.12	3.05	1.60	-0.47	3.71	1.68	-0.78	4.20
Adjusted model A	SO_2	0.20	-1.00	1.41	0.21	-1.01	1.44	0.27	-1.12	1.68
Adjusted model B	SO_2	0.02	-1.57	1.64	-0.33	-1.94	1.30	-0.21	-2.10	1.71
Adjusted model C	SO_2	0.10	-1.49	1.72	-0.31	-1.93	1.33	-0.12	-2.02	1.81
Adjusted model A	O_3	1.53	-0.41	3.51	0.70	-1.12	2.55	1.58	-0.68	3.90
Adjusted model C	O_3	1.31	-0.74	3.40	0.37	-1.55	2.32	1.16	-1.28	3.67

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3.

Stroke

In single pollutant models, each pollutant in relation to daily stroke hospitalizations was non-significant (Table 3.10). When multiple gaseous pollutants were included in the time-series model NO_2 lagged 1 day in relation to stroke hospitalizations was negative and statistically significant. The results were also negative and statistically significant when the mean of same day NO_2 and previous day NO_2 levels was modelled ($MPC_{\text{mean lag, adjusted C}}$= -4.13 percent, 95 percent CI: -7.96, -0.14). Other gaseous pollutant associations remained insignificant in multiple pollutant time-series models.

Table 3.11 shows no significant associations of CO, SO_2 and O_3 with daily stroke deaths. The association between NO_2 and stroke deaths was positive and statistically significant when the average between same day and previous day pollutant levels were modeled ($MPC_{\text{mean lag, adjusted A}}$=3.78 percent, 95 percent CI: 0.09, 7.61, $MPC_{\text{mean lag, adjusted B}}$ =6.40 percent, 95 percent CI: 1.03, 12.05, $MPC_{\text{mean lag, adjusted C}}$ =5.78 percent, 95 percent CI: 0.12, 11.76). Mean percent change estimates of NO_2 were also positive and statistically significant across all lag periods when models included weather conditions, SO_2 and CO.

Table 3.10 Mean percentage of change in daily stroke hospitalizations across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

Stroke Hospitalizations		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	**CO**	-0.53	-2.63	1.62	-0.53	-2.63	1.62	-0.66	-3.00	1.74
Adjusted model B	**CO**	-0.38	-3.52	2.86	0.80	-2.38	4.07	0.31	-3.32	4.09
Adjusted model C	**CO**	0.26	-3.03	3.65	1.27	-2.04	4.70	1.30	-2.57	5.32
Adjusted model A	**NO_2**	-0.82	-3.08	1.49	-2.04	-4.29	0.26	-1.86	-4.42	0.77
Adjusted model B	**NO_2**	-1.06	-4.24	2.24	**-3.45**	-6.56	-0.23	-3.07	-6.71	0.71
Adjusted model C	**NO_2**	-1.75	-5.07	1.67	**-3.95**	-7.18	-0.60	**-4.13**	-7.96	-0.14
Adjusted model A	**SO_2**	-0.01	-1.97	2.00	-0.01	-2.02	2.04	-0.01	-2.32	2.35
Adjusted model B	**SO_2**	0.77	-1.91	3.51	1.30	-1.44	4.12	1.47	-1.77	4.81
Adjusted model C	**SO_2**	0.89	-1.80	3.64	1.37	-1.38	4.19	1.67	-1.59	5.03
Adjusted model A	**O_3**	1.88	-1.20	5.06	0.69	-2.18	3.64	1.82	-1.77	5.55
Adjusted model C	**O_3**	2.30	-0.98	5.70	1.62	-1.45	4.78	3.10	-0.85	7.22

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3).
Statistically significant associations are shown in bold.

Figure 3.9 Mean percentage of change in daily stroke hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions

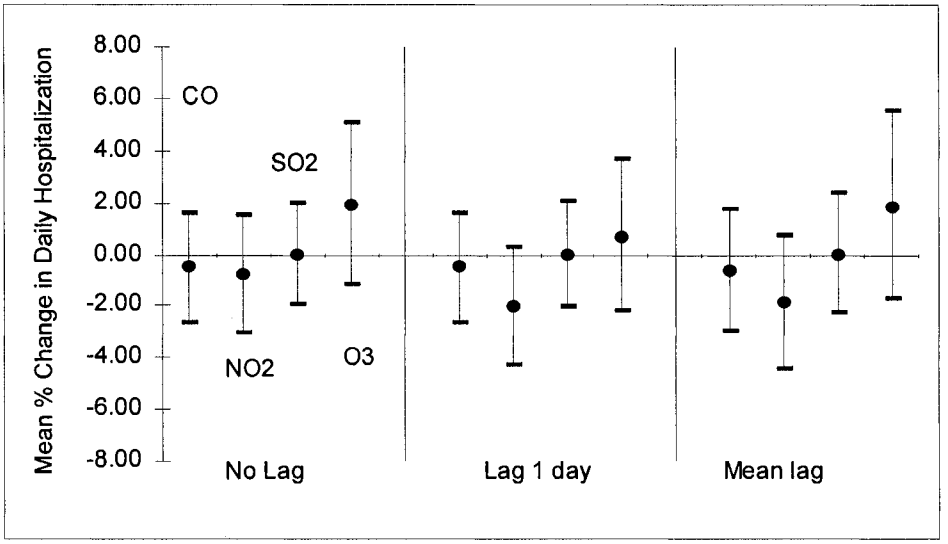


Figure 3.10 Mean percentage of change in daily stroke hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions and gaseous pollutants (CO, SO_2, NO_2 and O_3)

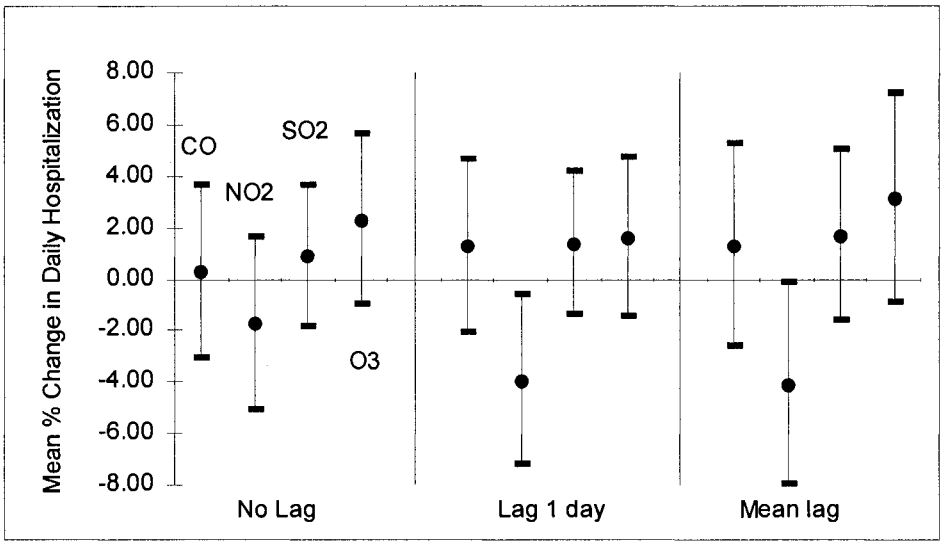


Table 3.11 Mean percentage of change in daily stroke deaths across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

Stroke Deaths		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	**CO**	0.38	-2.49	3.33	0.41	-2.45	3.35	0.49	-2.70	3.80
Adjusted model B	**CO**	-2.46	-6.57	1.83	-2.72	-6.81	1.56	-3.58	-8.24	1.32
Adjusted model C	**CO**	-2.02	-6.29	2.44	-2.51	-6.75	1.93	-3.10	-8.01	2.07
Adjusted model A	**NO_2**	2.87	-0.35	6.19	2.91	-0.31	6.23	**3.78**	0.09	7.61
Adjusted model B	**NO_2**	**4.75**	0.19	9.52	**4.59**	0.06	9.33	**6.40**	1.03	12.05
Adjusted model C	**NO_2**	4.21	-0.52	9.17	4.33	-0.38	9.28	**5.78**	0.12	11.76
Adjusted model A	**SO_2**	0.83	-1.87	3.60	1.18	-1.56	4.01	1.34	-1.81	4.58
Adjusted model B	**SO_2**	0.03	-3.52	3.72	0.64	-2.98	4.40	0.49	-3.74	4.92
Adjusted model C	**SO_2**	0.14	-3.43	3.84	0.68	-2.95	4.45	0.63	-3.64	5.08
Adjusted model A	**O_3**	2.79	-1.54	7.33	1.82	-2.23	6.05	3.32	-1.76	8.65
Adjusted model C	**O_3**	1.78	-2.76	6.54	0.79	-3.45	5.22	1.72	-3.69	7.43

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3).
Statistically significant associations are shown in bold.

Figure 3.11 Mean percentage of change in daily stroke deaths for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions

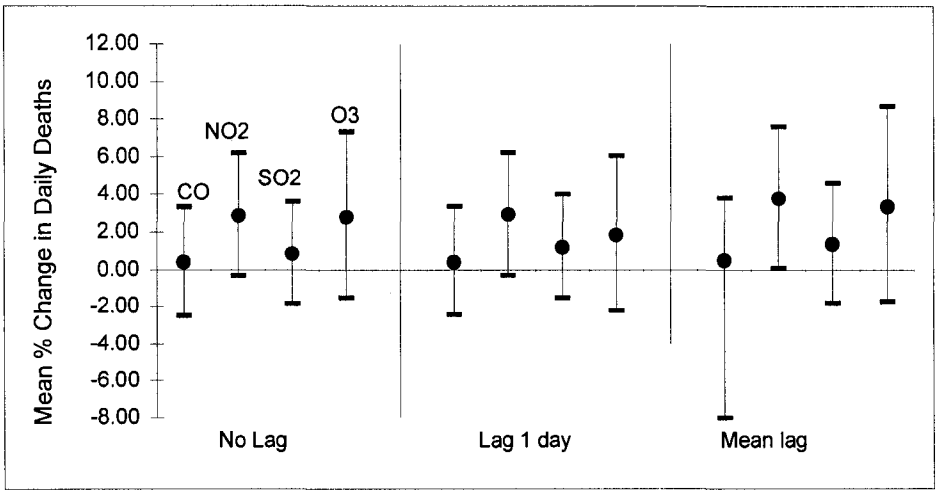
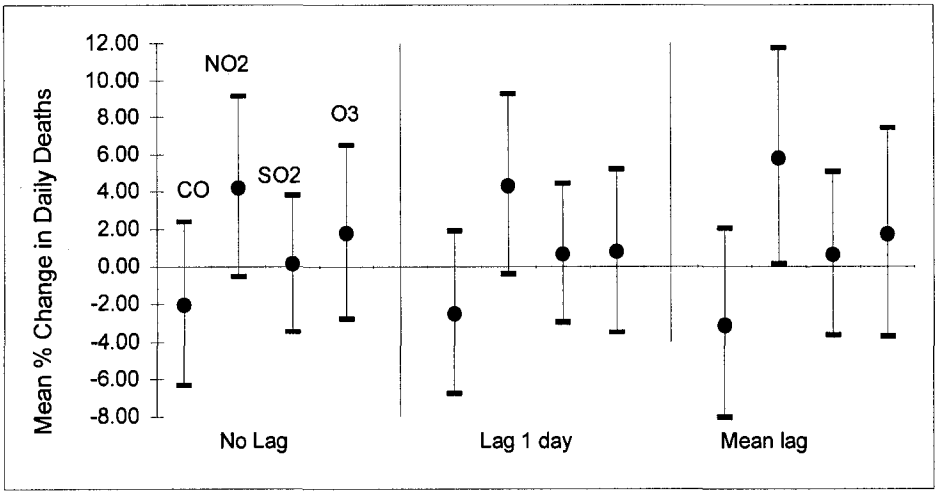


Figure 3.12 Mean percentage of change in daily stroke deaths for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions and gaseous pollutants (CO, SO_2, NO_2 and O_3)



Ischemic heart disease

There was a positive and statistically significant relationship between ischemic heart disease hospitalizations and CO for all adjusted models for same day and pollutant levels averaged between same day and previous day concentrations. The results in Table 3.12 also show a positive and statistically significant association of same day NO_2 pollutant levels with ischemic heart disease hospitalization, albeit a smaller association when compared to CO models and just for the single pollutant model ($MPC_{\text{no lag, adjusted A}}$= 1.18 percent, 95 percent CI: 0.10, 2.27). Other associations between the gaseous pollutants and ischemic heart disease hospitalizations were non-significant. Additionally, all models of the gaseous pollutants in relation to deaths due to ischemic heart disease were non-significant (Table 3.13).

Table 3.12 Mean percentage of change in daily ischemic heart disease hospitalizations across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

Ischemic Heart Disease Hospitalizations		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	CO	**1.76**	0.76	2.77	0.76	-0.23	1.76	**1.57**	0.46	2.70
Adjusted model B	CO	**2.42**	0.92	3.95	1.30	-0.19	2.82	**2.42**	0.69	4.18
Adjusted model C	CO	**2.31**	0.75	3.90	1.34	-0.21	2.91	**2.39**	0.56	4.25
Adjusted model A	NO_2	**1.18**	0.10	2.27	0.09	-0.98	1.18	0.83	-0.40	2.08
Adjusted model B	NO_2	0.10	-1.41	1.65	-0.90	-2.41	0.63	-0.55	-2.31	1.24
Adjusted model C	NO_2	0.23	-1.37	1.85	-0.94	-2.52	0.66	-0.51	-2.39	1.40
Adjusted model A	SO_2	0.46	-0.47	1.40	0.39	-0.57	1.35	0.57	-0.52	1.68
Adjusted model B	SO_2	-1.05	-2.29	0.21	0.05	-1.23	1.35	-0.72	-2.23	0.81
Adjusted model C	SO_2	-1.07	-2.32	0.20	0.05	-1.23	1.35	-0.72	-2.24	0.81
Adjusted model A	O_3	-0.77	-2.19	0.67	-0.29	-1.64	1.07	-0.76	-2.42	0.93
Adjusted model C	O_3	-0.39	-1.91	1.15	0.12	-1.31	1.57	-0.10	-1.92	1.75

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3).
Statistically significant associations are shown in bold.

Figure 3.13 Mean percentage of change in daily ischemic heart disease hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions

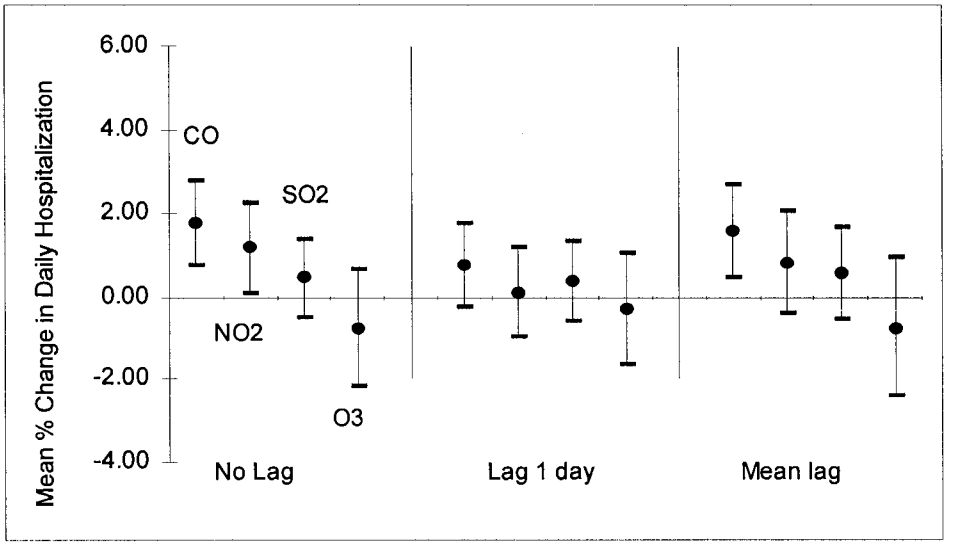


Figure 3.14 Mean percentage of change in daily ischemic heart disease hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions and gaseous pollutants (CO, SO_2, NO_2 and O_3)

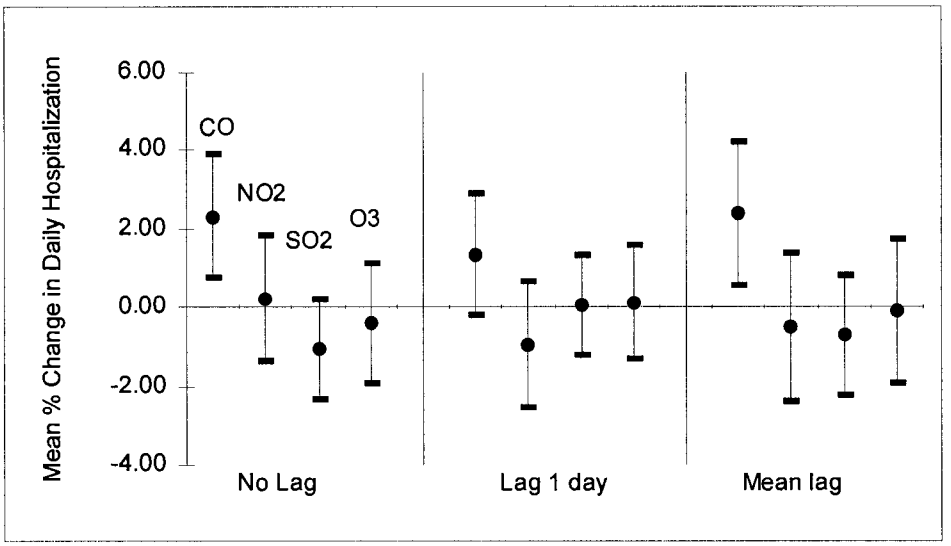


Table 3.13 Mean percentage of change in daily ischemic heart disease deaths across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

Ischemic Heart Disease Deaths		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	CO	0.40	-1.31	2.15	0.13	-1.58	1.87	0.33	-1.58	2.28
Adjusted model B	CO	0.67	-1.86	3.27	-0.11	-2.63	2.47	0.37	-2.54	3.37
Adjusted model C	CO	1.26	-1.37	3.97	-0.15	-2.75	2.53	0.80	-2.25	3.96
Adjusted model A	NO_2	0.52	-1.38	2.47	0.68	-1.23	2.63	0.79	-1.40	3.02
Adjusted model B	NO_2	0.76	-1.91	3.50	1.33	-1.35	4.09	1.43	-1.70	4.65
Adjusted model C	NO_2	0.06	-2.71	2.91	1.37	-1.42	4.25	0.91	-2.39	4.32
Adjusted model A	SO_2	-0.33	-1.94	1.31	-0.28	-1.92	1.39	-0.41	-2.28	1.50
Adjusted model B	SO_2	-1.09	-3.22	1.08	-0.85	-3.02	1.36	-1.36	-3.87	1.23
Adjusted model C	SO_2	-0.94	-3.08	1.24	-0.86	-3.03	1.35	-1.24	-3.77	1.36
Adjusted model A	O_3	2.27	-0.40	5.01	0.20	-2.27	2.74	1.71	-1.39	4.90
Adjusted model C	O_3	2.42	-0.41	5.33	-0.13	-2.73	2.55	1.57	-1.78	5.03

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3).

Acute myocardial infarction

Results in Table 3.14 show a positive and statistically significant association between CO and AMI hospitalizations when same day and mean pollutant concentrations were modeled in the single pollutant model ($MPC_{\text{no lag, adjusted A}}$= 2.73 percent, 95 percent CI: 0.58, 4.92, $MPC_{\text{mean lag, adjusted A}}$= 2.62 percent, 95 percent CI: 0.22, 5.07) and when further adjusted for SO_2 and NO_2 ($MPC_{\text{no lag, adjusted B}}$= 3.75 percent, 95 percent CI: 0.52, 7.10, $MPC_{\text{mean lag, adjusted B}}$= 4.04 percent, 95 percent CI: 0.30, 7.92). In contrast, ozone was associated with a negative and statistically significant percent change in AMI hospitalizations when ozone was lagged 1 day and when the average of same day and previous day ozone concentrations were modeled. There were no significant associations between any gaseous pollutants and AMI deaths (Table 3.15).

Table 3.14 Mean percentage of change in daily acute myocardial infarction hospitalizations across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

Acute Myocardial Infarction Hospitalizations		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	CO	**2.73**	0.58	4.92	1.47	-0.66	3.64	**2.62**	0.22	5.07
Adjusted model B	CO	**3.75**	0.52	7.10	2.54	-0.68	5.86	**4.04**	0.30	7.92
Adjusted model C	CO	3.20	-0.15	6.67	1.46	-1.85	4.88	2.72	-1.18	6.78
Adjusted model A	NO_2	0.86	-1.43	3.21	-0.52	-2.79	1.80	0.22	-2.38	2.89
Adjusted model B	NO_2	-2.34	-5.48	0.91	**-3.48**	-6.59	-0.28	**-3.98**	-7.57	-0.24
Adjusted model C	NO_2	-1.76	-5.06	1.65	-2.37	-5.64	1.02	-2.60	-6.48	1.44
Adjusted model A	SO_2	1.75	-0.24	3.77	1.48	-0.55	3.55	2.19	-0.15	4.59
Adjusted model B	SO_2	0.73	-1.93	3.47	1.77	-0.97	4.58	1.78	-1.45	5.12
Adjusted model C	SO_2	0.63	-2.03	3.37	1.62	-1.11	4.43	1.51	-1.72	4.85
Adjusted model A	O_3	-2.98	-5.92	0.05	**-4.32**	-7.06	-1.49	**-5.33**	-8.69	-1.85
Adjusted model C	O_3	-1.90	-5.05	1.37	**-3.55**	-6.48	-0.54	-3.94	-7.64	-0.09

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3).
Statistically significant associations are shown in bold.

Figure 3.15 Mean percentage of change in daily acute myocardial infarction hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions

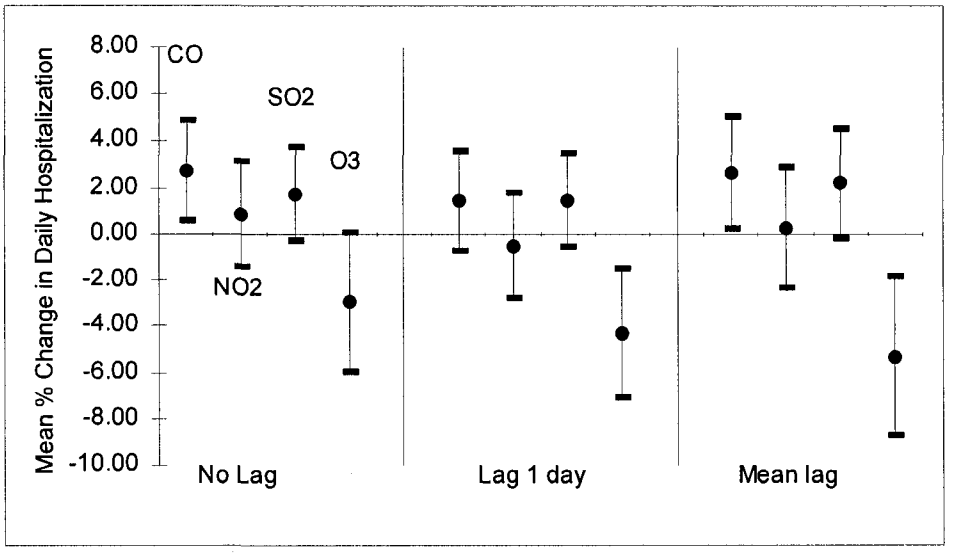


Figure 3.16 Mean percentage of change in daily acute myocardial infarction hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions and gaseous pollutants (CO, SO_2, NO_2 and O_3)

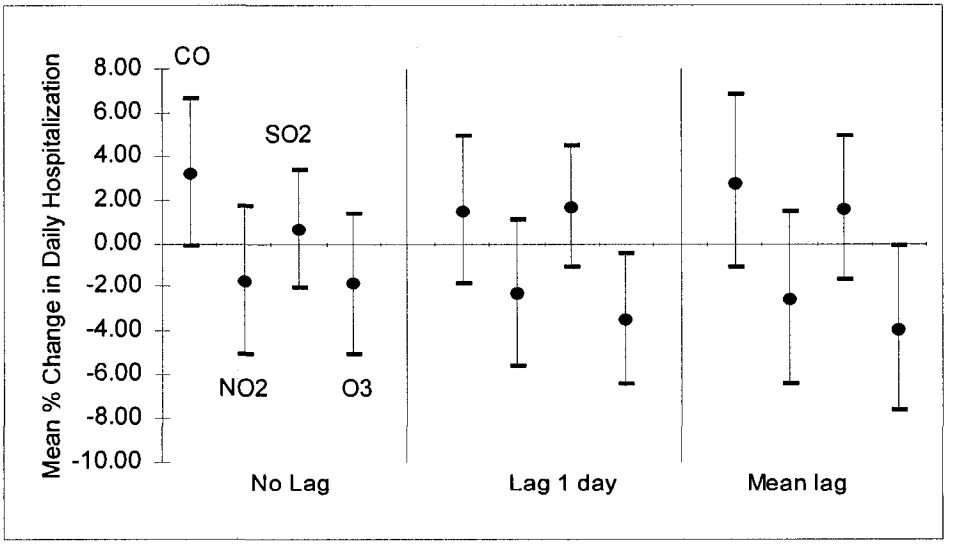


Table 3.15 Mean percentage of change in daily acute myocardial infarction deaths across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

Acute Myocardial Infarction Deaths		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	CO	0.44	-1.89	2.82	-0.77	-3.08	1.60	-0.21	-2.80	2.45
Adjusted model B	CO	0.12	-3.28	3.65	0.00	-3.43	3.54	0.09	-3.84	4.17
Adjusted model C	CO	0.30	-3.24	3.96	-0.73	-4.24	2.92	-0.40	-4.49	3.87
Adjusted model A	NO_2	0.40	-2.18	3.05	-1.22	-3.78	1.40	-0.54	-3.47	2.48
Adjusted model B	NO_2	-0.02	-3.61	3.70	-1.15	-4.70	2.53	-0.80	-4.94	3.53
Adjusted model C	NO_2	-0.23	-3.97	3.65	-0.30	-4.03	3.57	-0.22	-4.63	4.40
Adjusted model A	SO_2	0.56	-1.65	2.81	-0.67	-2.90	1.61	-0.06	-2.62	2.56
Adjusted model B	SO_2	0.50	-2.41	3.49	-0.11	-3.06	2.93	0.29	-3.17	3.87
Adjusted model C	SO_2	0.54	-2.38	3.54	-0.26	-3.21	2.79	0.16	-3.31	3.75
Adjusted model A	O_3	0.51	-3.05	4.20	-2.63	-5.90	0.75	-1.68	-5.75	2.56
Adjusted model C	O_3	0.71	-3.07	4.63	-2.79	-6.24	0.78	-1.74	-6.14	2.86

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3).

Heart failure

Larger mean percent change estimates were seen in the time-series models of heart failure in comparison to other cardiovascular conditions. In single pollutant models, the associations between CO, NO_2 and SO_2 and heart failure hospitalizations were positive and statistically significant across the three lag periods investigated. Ozone was not significantly associated in any time-series models. CO adjusted for other gaseous pollutants in relation to heart failure hospitalizations remained statistically significant when modeled with same day and average pollutant concentrations. By contrast SO_2 remained significant when adjusted for other gaseous pollutants when modeled with pollutant concentrations lagged one day. Similar to most other mortality results studied, the associations between each gaseous pollutant and heart failure deaths were non-significant (Table 3.17).

Table 3.16 Mean percentage of change in daily heart failure hospitalizations across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

Heart Failure Hospitalizations		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	CO	**4.26**	2.90	5.64	**2.81**	1.46	4.17	**4.41**	2.89	5.95
Adjusted model B	CO	**3.35**	1.33	5.41	1.69	-0.31	3.73	**2.99**	0.67	5.36
Adjusted model C	CO	**3.55**	1.45	5.70	2.07	-0.02	4.19	**3.55**	1.09	6.06
Adjusted model A	NO_2	**4.09**	2.61	5.59	**2.24**	0.78	3.72	**4.14**	2.45	5.85
Adjusted model B	NO_2	1.89	-0.16	3.97	-0.26	-2.27	1.78	1.07	-1.30	3.49
Adjusted model C	NO_2	1.67	-0.46	3.85	-0.66	-2.74	1.46	0.47	-2.03	3.03
Adjusted model A	SO_2	**2.53**	1.28	3.80	**2.79**	1.50	4.09	**3.59**	2.11	5.09
Adjusted model B	SO_2	-0.43	-2.09	1.25	**1.87**	0.15	3.62	1.03	-0.99	3.09
Adjusted model C	SO_2	-0.39	-2.06	1.30	**1.93**	0.21	3.69	1.15	-0.88	3.22
Adjusted model A	O_3	-0.02	-1.92	1.91	0.50	-1.30	2.32	0.37	-1.85	2.64
Adjusted model C	O_3	0.70	-1.33	2.76	1.29	-0.61	3.24	1.73	-0.71	4.24

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3).
Statistically significant associations are shown in bold.

Figure 3.17 Mean percentage of change in daily heart failure hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions

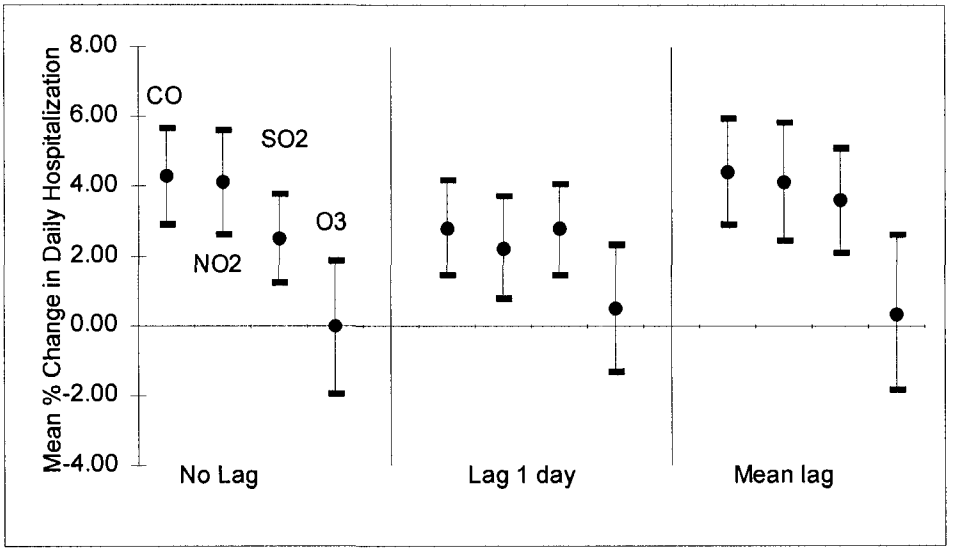


Figure 3.18 Mean percentage of change in daily heart failure hospitalizations for an increase in interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada, adjusted for weather conditions and gaseous pollutants (CO, SO_2, NO_2 and O_3)

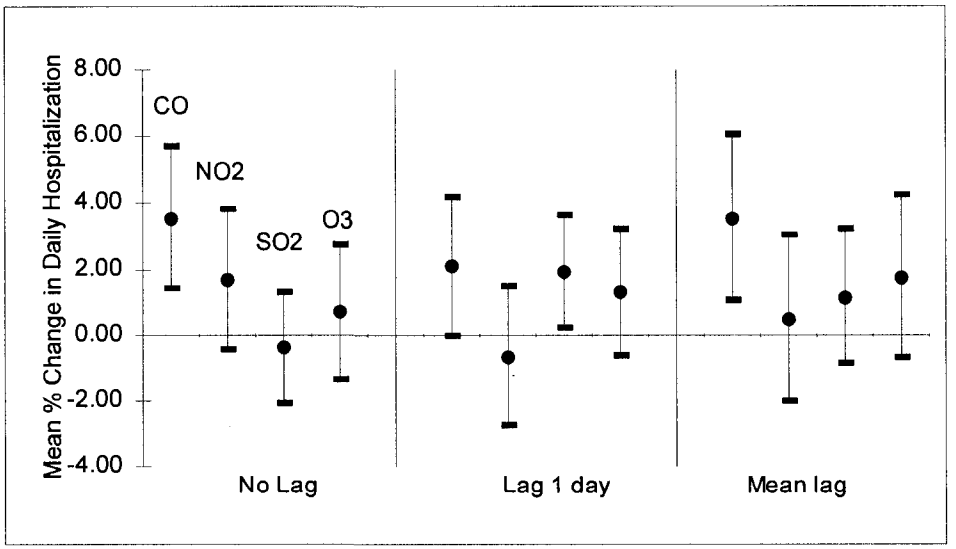


Table 3.17 Mean percentage of change in daily heart failure deaths across the interquartile range of lagged exposures to gaseous pollutants in the elderly in Vancouver, Canada

Heart Failure Deaths		Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Adjusted model A	CO	-1.55	-6.99	4.20	-0.57	-6.01	5.19	-1.32	-7.37	5.12
Adjusted model B	CO	-0.19	-8.21	8.53	-0.36	-8.33	8.30	-0.29	-9.43	9.77
Adjusted model C	CO	0.12	-8.20	9.20	-0.34	-8.59	8.66	0.03	-9.58	10.67
Adjusted model A	NO_2	-2.75	-8.47	3.32	-1.60	-7.40	4.56	-2.85	-9.37	4.14
Adjusted model B	NO_2	-3.35	-11.22	5.22	-2.88	-10.76	5.70	-4.26	-13.30	5.72
Adjusted model C	NO_2	-3.67	-11.82	5.23	-2.90	-11.08	6.02	-4.60	-14.10	5.95
Adjusted model A	SO_2	-0.71	-5.67	4.52	0.68	-4.41	6.04	-0.03	-5.79	6.08
Adjusted model B	SO_2	1.10	-5.64	8.32	2.36	-4.51	9.71	2.42	-5.63	11.16
Adjusted model C	SO_2	1.17	-5.59	8.42	2.36	-4.51	9.73	2.50	-5.59	11.29
Adjusted model A	O_3	0.57	-7.11	8.89	-0.46	-7.71	7.36	0.04	-8.84	9.78
Adjusted model C	O_3	1.15	-7.02	10.05	0.07	-7.62	8.40	1.05	-8.64	11.77

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2);
Adjusted model C, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2, and O_3).

Season-specific analysis for ozone

When modelled with year round data, there was a negative, statistically significant association between ozone and AMI when lagged one day or the average of same day and previous days' ozone levels. Associations between other cardiovascular conditions, when modeled with year round data were non-significant. Table 3.18 shows the results of the time-series analysis of ozone by warm and cool seasons. The negative and statistically signification association between ozone and AMI hospitalizations remained for the cool season; however, for the warm season and when the model was adjusted for other gaseous pollutants (CO, NO_2 and SO_2) the association was not significant. The same day concentration of ozone was negatively and significantly associated with overall cardiovascular hospitalizations during the warm season ($MPC_{\text{no lag, adjusted B}}$= -1.46 percent, 95 percent CI: -2.86, -0.04). Table 3.18 also shows positive associations with heart failure during the warm season when adjusted for weather conditions and during the cool season when adjusted for weather conditions and other gaseous pollutants.

Table 3.19 summarizes the results of ozone in relation to overall and specific cardiovascular deaths by warm and cool season modelled according to the NMMAPS methodology. The associations were not significant with the noted exception of the positive, statistically significant association between ozone and stroke deaths during the cool season when ozone levels were lagged one day ($MPC_{\text{lag 1 day, adjusted A}}$= 6.74 percent, 95 percent CI: 0.15, 13.76, $MPC_{\text{lag 1 day, adjusted B}}$= 8.22 percent, 95 percent CI: 0.68, 16.33). The equivalent association was not significant during the warm season.

Table 3.18 Mean percentage of change in daily cardiovascular hospitalizations across the interquartile range of lagged exposures to maximum 1-hour concentrations of ozone by warm and cool season in the elderly in Vancouver, Canada

Season	Hosps	Model	Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
			Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Warm	**All cardio**	Adjusted model A	-0.11	-1.35	1.15	-0.64	-1.78	0.51	-0.61	-2.08	0.88
	All cardio	Adjusted model B	**-1.46**	-2.86	-0.04	-0.30	-1.61	1.02	-1.43	-3.15	0.33
	Stroke	Adjusted model A	1.72	-2.20	5.81	-1.27	-4.81	2.40	0.15	-4.44	4.96
	Stroke	Adjusted model B	3.35	-1.22	8.12	-0.57	-4.62	3.65	1.95	-3.57	7.79
	IHD	Adjusted model A	-0.67	-2.49	1.17	-0.51	-2.18	1.20	-0.90	-3.05	1.30
	IHD	Adjusted model B	-1.44	-3.50	0.67	-0.03	-1.96	1.93	-1.09	-3.63	1.51
	AMI	Adjusted model A	-0.25	-4.12	3.77	-3.29	-6.78	0.32	-2.90	-7.38	1.78
	AMI	Adjusted model B	-1.43	-5.78	3.11	-2.83	-6.79	1.30	-3.62	-8.83	1.89
	Heart failure	Adjusted model A	**2.55**	0.02	5.14	2.01	-0.31	4.38	**3.49**	0.47	6.61
	Heart failure	Adjusted model B	0.74	-2.08	3.64	0.89	-1.71	3.55	1.20	-2.28	4.80
Cool	**All cardio**	Adjusted model A	-0.75	-2.19	0.71	0.89	-0.55	2.35	0.10	-1.53	1.76
	All cardio	Adjusted model B	0.59	-1.08	2.29	**2.01**	0.36	3.69	1.89	-0.05	3.86
	Stroke	Adjusted model A	0.15	-4.33	4.85	2.48	-2.05	7.22	1.71	-3.41	7.10
	Stroke	Adjusted model B	0.76	-4.40	6.21	3.69	-1.50	9.14	3.46	-2.59	9.89
	IHD	Adjusted model A	-0.89	-3.02	1.29	-0.18	-2.30	1.98	-0.68	-3.09	1.78
	IHD	Adjusted model B	0.28	-2.19	2.82	0.43	-1.98	2.90	0.61	-2.23	3.53
	AMI	Adjusted model A	**-6.17**	-10.36	-1.77	**-6.00**	-10.16	-1.66	**-7.77**	-12.42	-2.88
	AMI	Adjusted model B	-3.91	-8.83	1.28	-4.80	-9.56	0.21	-5.25	-10.80	0.64
	Heart failure	Adjusted model A	-1.49	-4.22	1.32	0.22	-2.52	3.04	-0.80	-3.90	2.39
	Heart failure	Adjusted model B	2.67	-0.61	6.05	**3.93**	0.71	7.26	**4.80**	0.98	8.76

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2).
Statistically significant associations are shown in bold.

Table 3.19 Mean percentage of change in daily cardiovascular deaths across the interquartile range of lagged exposures to maximum 1-hour concentrations of ozone by warm and cool season in the elderly in Vancouver, Canada

Season	Deaths	Model	Lag 0 days			Lag 1 day			Mean Lag (Lag 0 and Lag 1 day)		
			Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
Warm	**All cardio**	Adjusted model A	1.47	-1.01	4.02	0.75	-1.55	3.10	1.66	-1.30	4.71
	All cardio	Adjusted model B	1.21	-1.61	4.11	0.45	-2.16	3.12	1.24	-2.21	4.81
	Stroke	Adjusted model A	4.23	-1.41	10.19	-0.66	-5.67	4.61	2.41	-4.15	9.43
	Stroke	Adjusted model B	3.49	-2.87	10.26	-2.34	-7.93	3.58	0.18	-7.32	8.28
	IHD	Adjusted model A	1.79	-1.61	5.30	0.80	-2.33	4.04	1.93	-2.11	6.14
	IHD	Adjusted model B	1.42	-2.43	5.43	1.11	-2.46	4.81	1.97	-2.75	6.93
	AMI	Adjusted model A	-0.89	-5.39	3.82	-3.30	-7.40	0.98	-3.33	-8.54	2.17
	AMI	Adjusted model B	-0.72	-5.83	4.67	-2.43	-7.11	2.48	-2.59	-8.70	3.92
	Heart failure	Adjusted model A	-3.16	-12.70	7.42	-0.17	-9.38	9.98	-2.39	-13.72	10.43
	Heart failure	Adjusted model B	-1.41	-12.35	10.90	-1.36	-11.60	10.07	-1.87	-15.06	13.38
Cool	**All cardio**	Adjusted model A	1.69	-1.22	4.70	0.61	-2.23	3.53	1.47	-1.79	4.85
	All cardio	Adjusted model B	1.80	-1.54	5.24	0.75	-2.46	4.06	1.41	-2.38	5.36
	Stroke	Adjusted model A	2.51	-3.93	9.37	**6.74**	0.15	13.76	6.02	-1.44	14.05
	Stroke	Adjusted model B	2.89	-4.47	10.83	**8.22**	0.68	16.33	6.98	-1.76	16.49
	IHD	Adjusted model A	2.58	-1.45	6.77	-0.85	-4.68	3.13	1.06	-3.40	5.72
	IHD	Adjusted model B	3.19	-1.43	8.03	-1.12	-5.43	3.39	1.09	-4.09	6.54
	AMI	Adjusted model A	3.04	-2.44	8.83	-1.08	-6.26	4.37	1.19	-4.85	7.62
	AMI	Adjusted model B	4.81	-1.49	11.53	-2.72	-8.44	3.36	0.96	-5.99	8.42
	Heart failure	Adjusted model A	10.40	-1.95	24.30	2.51	-8.78	15.19	8.17	-5.32	23.57
	Heart failure	Adjusted model B	11.52	-2.81	27.95	2.15	-10.66	16.80	9.43	-6.51	28.09

Notes:
Adjusted model A, adjusted for daily weather conditions (mean temperature and mean dew point temperature);
Adjusted model B, adjusted for daily weather conditions and gaseous pollutants (CO, NO_2, SO_2).
Statistically significant associations are shown in bold.

3.4. Sensitivity Analysis

Time smoothing

The NMMAPS methodology utilized 7 degrees of freedom per year for smoothing time. Tables 3.20 and 3.21 show the results of the association between daily cardiovascular hospitalizations and deaths and each gaseous pollutant using various degrees of freedom to smooth the time component of the time-series. The results show models with less smoothing or more degrees of freedom for time had slightly larger mean percent change estimates.

Table 3.20 Mean percentage of change in daily cardiovascular hospitalizations across the interquartile range exposures to gaseous pollutants in the elderly in Vancouver, Canada, using different degrees of freedom to adjust for time

Pollutant	Degrees of freedom	Mean % of change	95% CI	
CO	4	**1.14**	0.10	2.19
	6	1.01	-0.04	2.08
	7 (NMMAPS model)	1.01	-0.04	2.08
	8	**1.07**	0.01	2.14
	10	**1.18**	0.11	2.27
	12	**1.18**	0.09	2.28
NO_2	4	**1.16**	0.09	2.25
	6	**1.35**	0.26	2.45
	7 (NMMAPS model)	**1.41**	0.31	2.51
	8	**1.44**	0.34	2.56
	10	**1.44**	0.32	2.56
	12	**1.43**	0.31	2.56
SO_2	4	-0.33	-1.17	0.51
	6	-0.28	-1.13	0.58
	7 (NMMAPS model)	-0.37	-1.22	0.49
	8	-0.41	-1.26	0.46
	10	-0.43	-1.30	0.44
	12	-0.41	-1.28	0.47
O_3	4	-0.46	-1.44	0.54
	6	-0.49	-1.51	0.54
	7 (NMMAPS model)	-0.49	-1.52	0.55
	8	-0.63	-1.66	0.41
	10	-0.39	-1.44	0.67
	12	-0.31	-1.36	0.76

Note:
Statistically significant associations are shown in bold.

Table 3.21 Mean percentage of change in daily cardiovascular deaths across the interquartile range exposures to gaseous pollutants in the elderly in Vancouver, Canada, using different degrees of freedom to adjust for time

Pollutant	Degrees of freedom	Mean % of change	95% CI	
CO	4	-0.19	-2.10	1.76
	6	-0.43	-2.37	1.54
	7 (NMMAPS model)	-0.47	-2.40	1.51
	8	-0.53	-2.47	1.45
	10	-0.72	-2.69	1.28
	12	-0.62	-2.62	1.41
NO_2	4	0.65	-1.34	2.69
	6	0.89	-1.15	2.97
	7 (NMMAPS model)	0.94	-1.12	3.05
	8	0.94	-1.13	3.05
	10	1.03	-1.06	3.17
	12	1.11	-1.00	3.26
SO_2	4	-0.02	-1.58	1.57
	6	0.05	-1.53	1.66
	7 (NMMAPS model)	0.10	-1.49	1.72
	8	0.04	-1.56	1.67
	10	0.23	-1.40	1.88
	12	0.18	-1.46	1.84
O_3	4	1.33	-0.64	3.35
	6	1.33	-0.72	3.41
	7 (NMMAPS model)	1.31	-0.74	3.40
	8	1.04	-1.01	3.14
	10	1.44	-0.65	3.58
	12	1.40	-0.71	3.55

Holidays

Smaller mean percent change estimates were seen in the time-series models that included an adjustment for statutory holidays. Table 3.22 shows the estimates of the associations between hospitalizations and gaseous pollutants when modeled using the NMMAPS multiple pollutant model in comparison to the NMMPAS multiple pollutant model with adjustment for holidays. The results show a positive, statistically significant relationship between NO_2 and all cardiovascular hospitalizations when modeled using the NMMAPS methodology ($MPC_{no\ lag}$ = 1.41 percent, 95 percent CI: 0.31, 2.51), however when the model included an adjustment for holidays the relationship was not statistically significant. Table 3.23 shows the comparison of estimates with and without adjustment for holidays for the relationship between cardiovascular deaths and gaseous pollutants. The mean percent change estimates with and without holidays were similar.

Table 3.22 Mean percentage of change in daily cardiovascular hospitalizations across the interquartile range of exposure to gaseous pollutants in the elderly in Vancouver, Canada, with and without adjustment for holidays

Hosps		NMMAPS multiple pollutant model			NMMAPS multiple pollutant model with adjustment for holidays		
		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	CO	1.01	-0.04	2.08	0.77	-0.29	1.83
	NO_2	**1.41**	0.31	2.51	0.34	-0.75	1.44
	SO_2	-0.37	-1.22	0.49	0.20	-0.66	1.07
	O_3	-0.49	-1.52	0.55	-0.20	-1.23	0.84
Stroke	CO	0.26	-3.03	3.65	0.19	-3.09	3.59
	NO_2	-1.75	-5.07	1.67	-2.03	-5.35	1.42
	SO_2	0.89	-1.80	3.64	1.04	-1.66	3.81
	O_3	2.30	-0.98	5.70	2.38	-0.91	5.78
IHD	CO	**2.31**	0.75	3.90	**2.09**	0.53	3.67
	NO_2	0.23	-1.37	1.85	-0.62	-2.22	1.00
	SO_2	-1.07	-2.32	0.20	-0.61	-1.86	0.67
	O_3	-0.39	-1.91	1.15	-0.15	-1.68	1.39
AMI	CO	3.20	-0.15	6.67	3.14	-0.22	6.60
	NO_2	-1.76	-5.06	1.65	-2.01	-5.32	1.42
	SO_2	0.63	-2.03	3.37	0.77	-1.91	3.52
	O_3	-1.90	-5.05	1.37	-1.83	-4.99	1.44
Heart failure	CO	**3.55**	1.45	5.70	**3.35**	1.25	5.50
	NO_2	1.67	-0.46	3.85	0.79	-1.34	2.96
	SO_2	-0.39	-2.06	1.30	0.09	-1.59	1.79
	O_3	0.70	-1.33	2.76	0.93	-1.10	3.01

Note:
Statistically significant associations are shown in bold.

Table 3.23 Mean percentage of change in daily cardiovascular deaths across the interquartile range of exposure to gaseous pollutants in the elderly in Vancouver, Canada, with and without adjustment for holidays

Deaths		NMMAPS multiple pollutant model			NMMAPS multiple pollutant model with adjustment for holidays		
		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	CO	-0.47	-2.40	1.51	-0.47	-2.41	1.50
	NO_2	0.94	-1.12	3.05	0.93	-1.15	3.05
	SO_2	0.10	-1.49	1.72	0.11	-1.49	1.74
	O_3	1.31	-0.74	3.40	1.31	-0.74	3.40
Stroke	CO	-2.02	-6.29	2.44	-1.95	-6.22	2.52
	NO_2	4.21	-0.52	9.17	4.42	-0.35	9.42
	SO_2	0.14	-3.43	3.84	0.03	-3.55	3.74
	O_3	1.78	-2.76	6.54	1.73	-2.81	6.49
IHD	CO	1.26	-1.37	3.97	1.21	-1.42	3.92
	NO_2	0.06	-2.71	2.91	-0.06	-2.84	2.81
	SO_2	-0.94	-3.08	1.24	-0.88	-3.02	1.31
	O_3	2.42	-0.41	5.33	2.45	-0.38	5.36
AMI	CO	0.30	-3.24	3.96	0.20	-3.33	3.87
	NO_2	-0.23	-3.97	3.65	-0.44	-4.19	3.46
	SO_2	0.54	-2.38	3.54	0.66	-2.27	3.68
	O_3	0.71	-3.07	4.63	0.76	-3.02	4.68
Heart failure	CO	0.12	-8.20	9.20	0.21	-8.12	9.30
	NO_2	-3.67	-11.82	5.23	-3.39	-11.61	5.60
	SO_2	1.17	-5.59	8.42	1.01	-5.77	8.27
	O_3	1.15	-7.02	10.05	1.09	-7.09	9.98

Weather

Tables 3.24 and 3.25 show the mean percent change estimates for multiple pollutant models with no lag with different weather adjustments.

NMMAPS multiple pollutant model:

- Log (E (Y)) = βX_i + DOW + S_1 (time, 7df/year) + S_2 ($temp_0$, 6df) + S_3 ($temp_{1-3}$, 6df) + S_4 (dew_0, 3df) + S_5 (dew_{1-3}, 3df)

NMMAPS multiple pollutant model with mean temperature only:

- Log (E (Y)) = βX_i + DOW + S_1 (time, 7df/year) + S_2 ($temp_0$, 6df) + S_3 ($temp_{1-3}$, 6df)

NMMAPS multiple pollutant model with mean dew point temperature only:

- Log (E (Y)) = βX_i + DOW + S_1 (time, 7df/year) + S_4 (dew_0, 3df) + S_5 (dew_{1-3}, 3df)

NMMAPS multiple pollutant model with no mean temperature adjustment and with the lagged dew point spline term replaced with a linear mean dew point temperature variable:

- Log (E (Y)) = βX_i + DOW + S_1 (time, 7df/year) + S_4 (dew_0, 3df) + αdew_{1-3}

The results in Table 3.24 show a positive and statistically significant association between AMI hospitalizations and CO when the multiple pollutant model only included dew point temperature, irrespective of whether or not a linear or spline adjustment was utilized. When adjusted with either temperature only or dew point temperature and mean temperature the results show a non-significant association. Table 3.25 shows a statistically significant association when either mean temperature or dew point temperature was used to adjust for weather in the relationship between NO_2 and stroke deaths. When both variables were used to adjust for weather conditions the relationship was not significant.

Table 3.24 Mean percentage of change in daily cardiovascular hospitalizations across the interquartile range of exposure to gaseous pollutants in the elderly in Vancouver, Canada, with different adjustments for weather conditions

Hosps		NMMAPS multiple pollutant model			Mean temperature only			Dew point temperature only			Linear dew point temperature only		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	CO	1.01	-0.04	2.08	1.02	-0.03	2.08	0.99	-0.06	2.05	0.96	-0.09	2.01
	NO_2	**1.41**	0.31	2.51	**1.40**	0.32	2.48	**1.12**	0.05	2.20	**1.12**	0.05	2.20
	SO_2	-0.37	-1.22	0.49	-0.36	-1.22	0.49	-0.28	-1.12	0.57	-0.21	-1.05	0.64
	O_3	-0.49	-1.52	0.55	-0.33	-1.28	0.63	-0.03	-0.90	0.85	-0.04	-0.91	0.84
Stroke	CO	0.26	-3.03	3.65	0.13	-3.12	3.49	0.15	-3.10	3.50	-0.04	-3.28	3.30
	NO_2	-1.75	-5.07	1.67	-1.63	-4.87	1.73	-1.92	-5.15	1.43	-1.80	-5.04	1.54
	SO_2	0.89	-1.80	3.64	0.94	-1.74	3.68	0.94	-1.71	3.67	1.14	-1.51	3.86
	O_3	2.30	-0.98	5.70	2.37	-0.68	5.51	1.37	-1.37	4.20	1.31	-1.43	4.13
IHD	CO	**2.31**	0.75	3.90	**2.23**	0.69	3.80	**2.17**	0.63	3.73	**2.14**	0.60	3.70
	NO_2	0.23	-1.37	1.85	0.54	-1.02	2.14	0.02	-1.53	1.61	0.03	-1.53	1.61
	SO_2	-1.07	-2.32	0.20	-1.07	-2.32	0.19	-0.93	-2.17	0.32	-0.88	-2.11	0.37
	O_3	-0.39	-1.91	1.15	-0.58	-1.98	0.84	0.07	-1.21	1.37	0.06	-1.22	1.36
AMI	CO	3.20	-0.15	6.67	2.95	-0.37	6.37	**3.41**	0.09	6.85	**3.29**	-0.03	6.71
	NO_2	-1.76	-5.06	1.65	-1.24	-4.49	2.12	-1.97	-5.19	1.37	-1.98	-5.21	1.35
	SO_2	0.63	-2.03	3.37	0.84	-1.83	3.57	0.49	-2.15	3.19	0.76	-1.87	3.46
	O_3	-1.90	-5.05	1.37	-1.99	-4.90	1.02	-0.99	-3.68	1.77	-1.04	-3.73	1.72
HF	CO	**3.55**	1.45	5.70	**3.48**	1.40	5.61	**3.58**	1.50	5.70	**3.59**	1.51	5.71
	NO_2	1.67	-0.46	3.85	1.70	-0.39	3.83	1.25	-0.83	3.37	1.27	-0.81	3.39
	SO_2	-0.39	-2.06	1.30	-0.44	-2.10	1.24	-0.29	-1.94	1.38	-0.34	-1.98	1.33
	O_3	0.70	-1.33	2.76	0.45	-1.42	2.35	0.59	-1.12	2.32	0.59	-1.11	2.32

Note: Statistically significant associations are shown in bold.

Table 3.25 Mean percentage of change in daily cardiovascular hospitalizations across the interquartile range of exposure to gaseous pollutants in the elderly in Vancouver, Canada, with different adjustments for weather conditions

Deaths		NMMAPS multiple pollutant model			Mean temperature only			Dew point temperature only			Linear dew point temperature only		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	CO	-0.47	-2.40	1.51	-0.42	-2.34	1.54	-0.18	-2.09	1.78	-0.23	-2.15	1.72
	NO_2	0.94	-1.12	3.05	1.34	-0.69	3.41	1.13	-0.90	3.19	1.14	-0.88	3.21
	SO_2	0.10	-1.49	1.72	0.07	-1.53	1.68	0.17	-1.41	1.78	0.24	-1.34	1.85
	O_3	1.31	-0.74	3.40	0.70	-1.19	2.62	1.40	-0.33	3.16	1.39	-0.34	3.14
Stroke	CO	-2.02	-6.29	2.44	-1.84	-6.08	2.58	-1.58	-5.81	2.84	-1.47	-5.70	2.96
	NO_2	4.21	-0.52	9.17	**5.00**	0.33	9.88	**4.84**	0.19	9.71	**4.89**	0.24	9.76
	SO_2	0.14	-3.43	3.84	-0.15	-3.70	3.54	-0.23	-3.76	3.43	-0.50	-4.01	3.14
	O_3	1.78	-2.76	6.54	-0.76	-4.88	3.53	-0.55	-4.30	3.34	-0.50	-4.25	3.39
IHD	CO	1.26	-1.37	3.97	1.26	-1.35	3.94	1.45	-1.16	4.12	1.39	-1.21	4.06
	NO_2	0.06	-2.71	2.91	0.54	-2.19	3.34	0.13	-2.58	2.92	0.10	-2.61	2.88
	SO_2	-0.94	-3.08	1.24	-0.93	-3.06	1.25	-0.94	-3.06	1.22	-0.78	-2.89	1.38
	O_3	2.42	-0.41	5.33	2.21	-0.41	4.90	2.02	-0.36	4.45	2.01	-0.37	4.44
AMI	CO	0.30	-3.24	3.96	0.21	-3.29	3.83	0.59	-2.90	4.21	0.45	-3.03	4.06
	NO_2	-0.23	-3.97	3.65	0.48	-3.20	4.31	0.12	-3.54	3.93	0.08	-3.58	3.88
	SO_2	0.54	-2.38	3.54	0.68	-2.24	3.69	0.45	-2.44	3.44	0.80	-2.10	3.78
	O_3	0.71	-3.07	4.63	0.43	-3.06	4.04	-0.12	-3.28	3.15	-0.15	-3.32	3.11
HF	CO	0.12	-8.20	9.20	-0.97	-9.16	7.95	-0.49	-8.71	8.46	-0.87	-9.04	8.03
	NO_2	-3.67	-11.82	5.23	-2.87	-10.94	5.94	-3.34	-11.37	5.41	-3.23	-11.26	5.52
	SO_2	1.17	-5.59	8.42	1.89	-4.90	9.16	2.35	-4.42	9.61	2.82	-3.96	10.07
	O_3	1.15	-7.02	10.05	2.47	-5.23	10.80	7.05	-0.28	14.92	6.97	-0.35	14.83

Note: Statistically significant associations are shown in bold.

Tables 3.26 and 3.27 show the comparison of mean percent change estimates of multiple pollutant models with the pollutant lagged 1 day (NMMAPS method) and models with the pollutants and weather variables lagged 1 day. A statistically significant association was seen between stroke deaths and NO_2 when both the pollutant and weather variables are lagged by 1 day (MPC = 5.16 percent, 95 percent CI: 0.39, 10.15). In contrast, when only the pollutants were lagged 1 day (according to the NMMAPS methodology) the relationship was not statistically significant (MPC = 4.33 percent, 95 percent CI: -0.38, 4.45).

Tables 3.28 and 3.29 show the comparison of estimates of multiple pollutant models with the mean pollutant concentration of current and previous days with non-lagged weather variables (NMMAPS method) versus models with the pollutant and weather variables lagged. A statistically significant, negative association was seen between NO_2 and stroke and between O_2 and AMI when only the mean pollutant concentration was included in the time-series model; however when the weather variables were lagged in the same manner as the pollutant concentrations the associations were non-significant.

Table 3.26 Mean percentage of change in daily cardiovascular hospitalizations across the interquartile range of exposure to gaseous pollutants lagged 1 day in the elderly in Vancouver, Canada, with and without lagged adjustments for weather conditions

Hosps		NMMAPS multiple pollutant model with pollutants lagged 1 day			NMMAPS multiple pollutant model with pollutant and weather variables lagged 1 day		
		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	CO	0.85	-0.21	1.92	0.85	-0.22	1.92
	NO_2	-1.06	-2.13	0.02	-0.93	-2.01	0.16
	SO_2	0.60	-0.28	1.48	0.81	-0.06	1.68
	O_3	0.27	-0.69	1.25	0.26	-0.77	1.30
Stroke	CO	1.27	-2.04	4.70	1.24	-2.08	4.68
	NO_2	**-3.95**	-7.18	-0.60	**-3.60**	-6.86	-0.22
	SO_2	1.37	-1.38	4.19	1.53	-1.18	4.30
	O_3	1.62	-1.45	4.78	2.42	-0.87	5.83
IHD	CO	1.34	-0.21	2.91	1.10	-0.45	2.68
	NO_2	-0.94	-2.52	0.66	-0.68	-2.27	0.94
	SO_2	0.05	-1.23	1.35	0.51	-0.76	1.79
	O_3	0.12	-1.31	1.57	-0.08	-1.60	1.46
AMI	CO	1.46	-1.85	4.88	0.84	-2.45	4.25
	NO_2	-2.37	-5.64	1.02	-2.07	-5.38	1.35
	SO_2	1.62	-1.11	4.43	2.09	-0.61	4.86
	O_3	**-3.55**	-6.48	-0.54	**-3.62**	-6.73	-0.41
Heart failure	CO	2.07	-0.02	4.19	2.08	-0.01	4.21
	NO_2	-0.66	-2.74	1.46	-0.60	-2.69	1.54
	SO_2	**1.93**	0.21	3.69	**1.87**	0.18	3.60
	O_3	1.29	-0.61	3.24	0.55	-1.47	2.61

Note:
Statistically significant associations are shown in bold.

Table 3.27 Mean percentage of change in daily cardiovascular deaths across the interquartile range of exposure to gaseous pollutants lagged 1 day in the elderly in Vancouver, Canada, with and without lagged adjustments for weather conditions

Deaths		NMMAPS multiple pollutant model with pollutants lagged 1 day			NMMAPS multiple pollutant model with pollutant and weather variables lagged 1 day		
		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	CO	-0.39	-2.32	1.59	-0.33	-2.27	1.65
	NO_2	1.60	-0.47	3.71	2.00	-0.08	4.13
	SO_2	-0.31	-1.93	1.33	-0.12	-1.72	1.50
	O_3	0.37	-1.55	2.32	0.81	-1.23	2.90
Stroke	CO	-2.51	-6.75	1.93	-2.36	-6.62	2.08
	NO_2	4.33	-0.38	9.28	**5.16**	0.39	10.15
	SO_2	0.68	-2.95	4.45	0.83	-2.76	4.55
	O_3	0.79	-3.45	5.22	0.79	-3.71	5.50
IHD	CO	-0.15	-2.75	2.53	-0.13	-2.74	2.55
	NO_2	1.37	-1.42	4.25	1.34	-1.47	4.23
	SO_2	-0.86	-3.03	1.35	-0.75	-2.89	1.44
	O_3	-0.13	-2.73	2.55	0.95	-1.85	3.82
AMI	CO	-0.73	-4.24	2.92	-0.85	-4.36	2.80
	NO_2	-0.30	-4.03	3.57	0.33	-3.44	4.25
	SO_2	-0.26	-3.21	2.79	-0.08	-3.01	2.93
	O_3	-2.79	-6.24	0.78	-2.25	-5.93	1.57
Heart failure	CO	-0.34	-8.59	8.66	-0.33	-8.59	8.68
	NO_2	-2.90	-11.08	6.02	-1.03	-9.38	8.09
	SO_2	2.36	-4.51	9.73	3.19	-3.64	10.51
	O_3	0.07	-7.62	8.40	-1.71	-9.68	6.96

Note:
Statistically significant associations are shown in bold.

Table 3.28 Mean percentage of change in daily cardiovascular hospitalizations across the interquartile range of mean lagged exposure to gaseous pollutants in the elderly in Vancouver, Canada, with and without lagged adjustments for weather conditions

Hosps		NMMAPS multiple pollutant model (pollutant mean lag)			NMMAPS multiple pollutant model (pollutant and weather mean lag)		
		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	CO	1.14	-0.10	2.40	1.15	-0.09	2.40
	NO_2	0.21	-1.08	1.51	0.25	-1.04	1.56
	SO_2	0.18	-0.86	1.22	0.24	-0.80	1.28
	O_3	-0.08	-1.31	1.17	-0.14	-1.41	1.14
Stroke	CO	1.30	-2.57	5.32	1.42	-2.45	5.44
	NO_2	**-4.13**	-7.96	-0.14	-3.96	-7.81	0.04
	SO_2	1.67	-1.59	5.03	1.70	-1.55	5.05
	O_3	3.10	-0.85	7.22	3.51	-0.57	7.76
IHD	CO	**2.39**	0.56	4.25	**2.21**	0.39	4.07
	NO_2	-0.51	-2.39	1.40	-0.39	-2.27	1.53
	SO_2	-0.72	-2.24	0.81	-0.52	-2.03	1.01
	O_3	-0.10	-1.92	1.75	-0.27	-2.13	1.63
AMI	CO	2.72	-1.18	6.78	2.29	-1.59	6.33
	NO_2	-2.60	-6.48	1.44	-2.47	-6.36	1.57
	SO_2	1.51	-1.72	4.85	1.87	-1.36	5.20
	O_3	**-3.94**	-7.64	-0.09	-3.79	-7.59	0.17
Heart failure	CO	**3.55**	1.09	6.06	**3.57**	1.11	6.08
	NO_2	0.47	-2.03	3.03	0.43	-2.07	2.99
	SO_2	1.15	-0.88	3.22	1.04	-0.98	3.10
	O_3	1.73	-0.71	4.24	1.08	-1.42	3.63

Note:
Statistically significant associations are shown in bold.

Table 3.29 Mean percentage of change in daily cardiovascular deaths across the interquartile range of mean lagged exposure to gaseous pollutants in the elderly in Vancouver, Canada, with and without lagged adjustments for weather conditions

Deaths		NMMAPS multiple pollutant model (pollutant mean lag)			NMMAPS multiple pollutant model (pollutant and weather mean lag)		
		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	CO	-0.56	-2.82	1.74	-0.51	-2.76	1.80
	NO_2	1.68	-0.78	4.20	1.94	-0.52	4.47
	SO_2	-0.12	-2.02	1.81	-0.07	-1.96	1.86
	O_3	1.16	-1.28	3.67	1.26	-1.25	3.83
Stroke	CO	-3.10	-8.01	2.07	-3.00	-7.90	2.17
	NO_2	**5.78**	0.12	11.76	**6.48**	0.78	12.50
	SO_2	0.63	-3.64	5.08	0.70	-3.55	5.14
	O_3	1.72	-3.69	7.43	1.78	-3.76	7.64
IHD	CO	0.80	-2.25	3.96	0.77	-2.29	3.92
	NO_2	0.91	-2.39	4.32	0.96	-2.34	4.38
	SO_2	-1.24	-3.77	1.36	-1.13	-3.65	1.47
	O_3	1.57	-1.78	5.03	2.24	-1.21	5.81
AMI	CO	-0.40	-4.49	3.87	-0.48	-4.56	3.78
	NO_2	-0.22	-4.63	4.40	0.24	-4.20	4.89
	SO_2	0.16	-3.31	3.75	0.34	-3.12	3.93
	O_3	-1.74	-6.14	2.86	-1.30	-5.82	3.44
Heart failure	CO	0.03	-9.58	10.67	0.78	-8.88	11.46
	NO_2	-4.60	-14.10	5.95	-4.27	-13.80	6.31
	SO_2	2.50	-5.59	11.29	2.20	-5.85	10.94
	O_3	1.05	-8.64	11.77	-0.92	-10.66	9.88

Note:
Statistically significant associations are shown in bold.

Tables 3.29a and 3.29b show the results of models with and without adjustment for PM. The tables show the results from the complete study period (January 1, 1985 to March 31, 1999) and the truncated study period when daily PM data were available (January 1, 1994 to March 31, 1999). The significant associations with and without PM_{10} in the truncated study period were the same (all cardiovascular hospitalizations and SO_2, ischemic heart disease and SO_2 and heart failure and CO) although the statistically significant negative relationships with SO_2 were not seen in the analysis results of the complete study period. PM_{10} was not significantly associated with any cardiovascular condition. When $PM_{2.5}$ was included in a multiple pollutant model in association with all cardiovascular hospitalizations, a positive and statistically significant association was seen with NO_2 and negative associations were seen with SO_2 and $PM_{2.5}$. All other associations were not statistically significant.

Table 3.30b shows a statistically significant association between CO and heart failure deaths during the truncated study period where PM data was available. The relationship was the only statistically significant between the gaseous or PM pollutants and cardiovascular deaths.

Table 3.30a Mean percentage of change in daily cardiovascular, stroke and IHD hospitalizations across the interquartile range of exposure to gaseous pollutants in the elderly in Vancouver, Canada, with and without adjustment for PM

Hosps		NMMAPS multiple pollutant model (Jan 1, 85 - March 31, 99)			Without PM (Jan 1, 94 - Mar 31, 99)			With PM_{10} adjustment (Jan 1, 94 - Mar 31, 99)			With $PM_{2.5}$ adjustment (Jun 1, 95 - March 31, 99)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	**CO**	1.01	-0.04	2.08	1.69	-1.14	4.60	2.17	-0.78	5.22	2.10	-1.32	5.64
	NO_2	**1.41**	0.31	2.51	1.40	-0.59	3.42	1.98	-0.25	4.26	**2.80**	0.13	5.55
	SO_2	-0.37	-1.22	0.49	**-2.33**	-3.97	-0.65	**-2.13**	-3.82	-0.42	**-2.45**	-4.61	-0.24
	O_3				-0.69	-2.38	1.02	-0.59	-2.29	1.13	-0.58	-2.58	1.46
	PM	-0.49	-1.52	0.55				-1.03	-2.76	0.74	**-1.99**	-3.20	-0.76
Stroke	**CO**	0.26	-3.03	3.65	7.16	-2.00	17.18	7.42	-2.11	17.87	5.46	-5.29	17.43
	NO_2	-1.75	-5.07	1.67	-4.31	-10.11	1.85	-4.04	-10.49	2.88	-3.95	-11.61	4.37
	SO_2	0.89	-1.80	3.64	-3.22	-8.30	2.15	-3.12	-8.31	2.35	-2.27	-8.96	4.91
	O_3				3.29	-2.13	9.01	3.34	-2.11	9.10	3.52	-2.93	10.39
	PM	2.30	-0.98	5.70				-0.52	-5.91	5.17	-2.60	-6.38	1.33
IHD	**CO**	**2.31**	0.75	3.90	1.73	-2.60	6.24	2.11	-2.40	6.83	1.59	-3.65	7.12
	NO_2	0.23	-1.37	1.85	1.13	-1.90	4.24	1.60	-1.80	5.10	1.15	-2.92	5.39
	SO_2	-1.07	-2.32	0.20	**-2.87**	-5.36	-0.30	**-2.71**	-5.26	-0.09	-1.70	-5.06	1.78
	O_3	-0.39	-1.91	1.15	-0.18	-2.77	2.48	-0.11	-2.71	2.57	-1.30	-4.36	1.87
	PM							-0.83	-3.49	1.91	-0.90	-2.79	1.04

Note:
Statistically significant associations are shown in bold.

Table 3.30b Mean percentage of change in daily AMI and heart failure hospitalizations across the interquartile range of exposure to gaseous pollutants in the elderly in Vancouver, Canada, with and without adjustment for PM

Hosps		NMMAPS multiple pollutant model (Jan 1, 85 - March 31, 99)			Without PM (Jan 1, 94 - Mar 31, 99)			With PM_{10} adjustment (Jan 1, 94 - Mar 31, 99)			With $PM_{2.5}$ adjustment (Jun 1, 95 - March 31, 99)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
AMI	**CO**	3.20	-0.15	6.67	-4.92	-13.10	4.04	-4.96	-13.46	4.37	-5.61	-15.52	5.46
	NO_2	-1.76	-5.06	1.65	1.57	-4.62	8.16	1.50	-5.36	8.87	3.16	-5.23	12.29
	SO_2	0.63	-2.03	3.37	2.04	-3.23	7.60	2.02	-3.35	7.69	-1.36	-8.17	5.95
	O_3	-1.90	-5.05	1.37	-0.83	-6.07	4.70	-0.84	-6.10	4.72	-3.22	-9.31	3.28
	PM							0.11	-5.33	5.87	-1.79	-5.64	2.23
HF	**CO**	**3.55**	1.45	5.70	**6.96**	1.39	12.83	**6.54**	0.77	12.64	6.51	-0.21	13.70
	NO_2	1.67	-0.46	3.85	0.10	-3.60	3.94	-0.37	-4.47	3.90	1.09	-3.90	6.33
	SO_2	-0.39	-2.06	1.30	-0.83	-3.98	2.43	-0.99	-4.19	2.33	-0.71	-4.89	3.65
	O_3	0.70	-1.33	2.76	2.33	-1.00	5.76	2.24	-1.10	5.69	2.28	-1.66	6.38
	PM							0.85	-2.48	4.30	-2.50	-4.81	-0.13

Note:
Statistically significant associations are shown in bold.

Table 3.31a Mean percentage of change in daily cardiovascular, stroke and IHD deaths across the interquartile range of exposure to gaseous pollutants in the elderly in Vancouver, Canada, with and without adjustment for PM

Deaths		NMMAPS multiple pollutant model (Jan 1, 85 - Dec 31, 98)			Without PM (Jan 1, 94 - Dec 31, 98)			With PM_{10} adjustment (Jan 1, 94 - Dec 31, 98)			With $PM_{2.5}$ adjustment (Jun 1, 95 - Dec 31, 98)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	**CO**	-0.47	-2.40	1.51	1.39	-4.44	7.58	0.51	-5.50	6.91	0.63	-6.26	8.04
	NO_2	0.94	-1.12	3.05	2.53	-1.62	6.86	1.49	-3.07	6.27	3.21	-2.37	9.10
	SO_2	0.10	-1.49	1.72	0.17	-3.34	3.80	-0.19	-3.74	3.50	0.07	-4.48	4.83
	O_3	1.31	-0.74	3.40	1.21	-2.37	4.93	1.04	-2.56	4.76	-0.10	-4.26	4.23
	PM							1.89	-1.80	5.72	-0.41	-2.88	2.13
Stroke	**CO**	-2.02	-6.29	2.44	-2.96	-14.78	10.49	-2.16	-14.52	11.99	1.39	-12.96	18.09
	NO_2	4.21	-0.52	9.17	4.36	-4.74	14.33	5.39	-4.78	16.65	3.41	-8.30	16.62
	SO_2	0.14	-3.43	3.84	5.86	-2.00	14.35	6.22	-1.81	14.92	4.44	-5.46	15.38
	O_3	1.78	-2.76	6.54	-3.27	-10.58	4.64	-3.10	-10.46	4.85	-8.07	-16.18	0.81
	PM							-1.78	-9.47	6.56	-3.81	-8.96	1.64
IHD	**CO**	1.26	-1.37	3.97	-2.09	-9.96	6.46	-3.47	-11.52	5.33	-6.24	-15.27	3.74
	NO_2	0.06	-2.71	2.91	3.77	-2.10	10.00	2.08	-4.32	8.90	6.14	-1.91	14.86
	SO_2	-0.94	-3.08	1.24	0.59	-4.34	5.76	0.01	-4.98	5.26	3.13	-3.43	10.13
	O_3	2.42	-0.41	5.33	3.97	-1.20	9.41	3.67	-1.50	9.12	4.60	-1.51	11.10
	PM							3.08	-2.13	8.58	-0.32	-3.83	3.31

Note:
Statistically significant associations are shown in bold.

Table 3.31b Mean percentage of change in daily AMI and heart failure deaths across the interquartile range of exposure to gaseous pollutants in the elderly in Vancouver, Canada, with and without adjustment for PM

Deaths		NMMAPS multiple pollutant model (Jan 1, 85 - Dec 31, 98)			Without PM (Jan 1, 94 - Dec 31, 98)			With PM_{10} adjustment (Jan 1, 94 - Dec 31, 98)			With $PM_{2.5}$ adjustment (Jun 1, 95 - Dec 31, 98)		
		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI		Mean % of change	95 % CI	
All cardio	**CO**	0.30	-3.24	3.96	-7.91	-17.85	3.22	-9.95	-20.04	1.42	-11.15	-22.45	1.80
	NO_2	-0.23	-3.97	3.65	4.34	-3.61	12.95	1.68	-6.89	11.03	7.58	-3.28	19.66
	SO_2	0.54	-2.38	3.54	3.65	-3.14	10.92	2.73	-4.12	10.08	6.39	-2.52	16.11
	O_3	0.71	-3.07	4.63	1.88	-4.94	9.18	1.43	-5.39	8.73	0.72	-7.15	9.27
	PM							4.88	-2.25	12.52	0.71	-4.01	5.66
Stroke	**CO**	0.12	-8.20	9.20	**25.62**	0.44	57.11	**28.85**	2.09	62.62	25.59	-4.44	65.06
	NO_2	-3.67	-11.82	5.23	-2.59	-16.45	13.56	0.39	-15.47	19.22	-4.64	-22.63	17.53
	SO_2	1.17	-5.59	8.42	-7.48	-19.13	5.85	-6.59	-18.53	7.11	-10.76	-25.41	6.77
	O_3	1.15	-7.02	10.05	6.45	-6.94	21.76	7.09	-6.46	22.60	7.62	-8.34	26.35
	PM							-5.26	-17.56	8.88	-1.10	-9.98	8.66

Note:
Statistically significant associations are shown in bold.

4. CHAPTER 4 DISCUSSION

4.1. General

The present study investigated the associations of short-term exposure to gaseous air pollutants including CO, NO_2, SO_2 and O_3 with overall and specific cardiovascular hospitalizations and deaths in the elderly population in Vancouver, Canada. During the study period ambient air pollution levels in Vancouver were relatively low compared to the Canadian National Ambient Air Quality Objectives maximum acceptable levels.

4.2. Strengths of this study

Strengths of this study include the large and complete dataset and the modelling methodology. Daily hospitalization and death data for the Vancouver area were extracted from the British Columbia Linked Dataset for a 13-year study period. Previous time-series analyses have been completed on study periods as short as one year.(49) Hospitalization, death and air pollution data were available for the complete study period. With data from Environment Canada, weather data were also available for the entire study period, therefore neither estimation nor imputation were required for the study. The long study period and completeness of the data increase the power of the study.

This project utilized the modelling methodology of the respected National Morbidity, Mortality and Air Pollution Study. The NMMAPS model has previously been applied to data from a wide variety of cities and climatic regions. There have been a variety of air pollution and morbidity or mortality time-series models published. The NMMAPS model utilized for this evaluation was selected over others since it appears to be widely accepted. Previous studies have reported concerns over biased relative risk estimates

due to the use of default S-plus parameters and locally weighted regression compared to natural splines.(58) The NMMAPS methodology addressed these issues through the use of natural splines to control for the effects of weather and time trends. Furthermore the degrees of freedoms were specified for each spline function. The application of the NMMAPS model addressed the major sources of confounding in time-series studies including temporal, weather and day of week trends.

4.3. Potential limitations and future work

Restricting the hospitalization counts to urgent and emergent admissions was intended to produce more accurate exposure measurements for the time-series analysis. Planned hospital admissions were excluded to avoid overestimation of the outcome measure. Specific data quality information was not available for the Vancouver hospitalization or death data, however other studies have reported on the accuracy of diagnostic coding.(91-94) One study specific to acute myocardial infarction reported a positive predictive value (PPV) of AMI to be over 95%, while another study reported a PPV of heart failure from coding of administrative records to be 88.6%.(91, 93)

Studies have also reported that cardiovascular conditions on death certificates are reasonably accurate (over 80%).(95, 96) Although one study reported that the accuracy of death certificate coding decreased as the age of the decedent increased, the accuracy across the three decades of the study did not change significantly.(95) While the American study reported less accurate stroke diagnoses (approximately 63%) a Japanese study found the accuracy of death certificates with stroke more accurate than those specifying cardiac diseases as an underlying cause of death; 84% and 66% respectively.(96) Even though potential inaccuracies in diagnostic coding exist, it was

assumed that inaccuracies in coding the cardiovascular conditions under review were distributed across the study period and any miscoding is unlikely to be associated with the daily levels of gaseous air pollutants.

Ecological studies are frequently limited to the use of ambient levels of air pollution due to the unavailability of person-level exposure data. Zeger et al. described two extremes of measurement error. The first type is referred to as the classic error model. In this model, the measured concentration (z) is an imperfect representation of the actual pollutant concentration (x). In this type of model, the measurement error (z-x) is uncorrelated with the true pollutant concentration (x). Opposite of the classic error model is the Berkson error model. In this model, z represents a pollutant concentration that is shared across a group of individuals whose exposure x varies because of indoor and outdoor activity differences. Based on models meant to simulate the two types of errors, the authors suggest that the Berkson errors likely create less biased estimates, whereas the classic error model may raise more concerns.(97) Studies examining the association between ambient and personal exposure levels of pollutants have reported varying results. Results varied by location, household characteristics, types of ventilation and the amount of time spent outdoors.(98-102) A recent study reported a significant, but low association between ambient and personal levels of exposure to gaseous air pollution with the exception of SO_2 in the summertime. A stronger association was reported between ambient and personal concentrations of NO_2 during the fall. The study also reported that ambient and personal pollution associations were stronger in high ventilation buildings.(99) Given that person-level pollution

concentrations were unavailable, ambient levels were an acceptable alternative for this study.

In time-series studies, only factors that vary in time over a short period of time can confound the observed association.(103) Cardiovascular risk factors, which are biologically meaningful, such as smoking and high blood pressure are unlikely to vary over days or weeks and therefore are not confounders in the relationship under investigation. They may potentially be effect modifiers. Individual data of cardiovascular risk factors were not available for the current study but future studies could consider the potential impact of individual's cardiovascular risk factors.

Research has suggested that studies utilizing community average exposure concentration may underestimate the health effects of air pollution.(104-106) Studies suggest the health effects of air pollution are diluted when community pollutant concentration averages are utilizes as opposed to pollutant levels from sources or monitoring stations closest to each individual. A Los Angeles based study reported the health effects were almost three times greater when analyses were based on pollutant concentrations close to individuals versus community pollutant levels.(104) For this study, community average pollutant concentrations and aggregate hospitalization and death data were utilized due to the unavailability of alternative information. Future analyses may be able to utilize pollutant measurements from the five to 31 monitoring stations within Greater Vancouver linked with individual home locations, possibly resulting in stronger associations.

Given that multiple pollutants can be created by the same combustion process it is a challenge in air pollution studies to separate the effect of one pollutant from another and address the possibility that one pollutant is acting as a surrogate for another pollutant. Multi-pollutant models were used in this study to try and tackle these issues, however the results are open to the same interpretation as single-pollutant models.(97) For example, if pollutant A is correlated with pollutant B, the results of both the single and multi-pollutant models could show the pollutant B as significant even if pollutant A is the exposure variable truly associated with the outcome of interest. Pollutant B may also be acting as a surrogate for pollutant A. Additionally, random misclassification of the exposure variables may lead to underestimation of the association with hospitalization or death.

4.4. Summary of findings and explanations

In the present study, the results have shown that exposure to gaseous pollutants (CO, NO_2, SO_2 and O_3) were significantly associated with overall and specific cardiovascular conditions. Several associations remained after adjusting for other gaseous pollutants.

There are similarities between the result of this study and previously reported studies. Several other studies have reported associations between CO, SO_2 or NO_2 and cardiovascular hospitalizations in single pollutant models.(49, 50, 65) When adjusted for other pollutants, Sunyer et al. reported non-significant associations between SO_2 and cardiovascular admissions,(50) which is also seen in this study's results. However similar comparisons could not be made with the other pollutants or studies as multiple-pollutant results were not reported. In this study, after adjusting for other pollutants only the association between same day NO_2 exposure and cardiovascular hospital

admissions remained significant with a mean percent change of 1.41 (95 percent CI: 0.31, 2.51). This suggests that reporting conclusions of significant associations solely based on single-pollutant models may be inappropriate. Considering the high correlation between pollutants, especially CO and NO_2 (r = 0.72), adjustments for other pollutants might underestimate the effect of a pollutant of interest.

This study found a strong association between same-day and average same-day and previous day's CO levels and ischemic heart disease hospitalizations. A study based in Detroit reported a relative risk of 1.010 (95 percent CI: 1.001, 1.018) for an interquartile range (1.28 ppm) increase of CO in association with IHD, unadjusted for other pollutants.(41) This study found a larger relative risk of 1.017 (95 percent CI: 1.010, 1.024) for an interquartile range (0.56 ppm) increase of CO in association with IHD. The association remained strong and the relative risk estimates increased when the association was adjusted for other gaseous pollutants. In Detroit, the association became non-significant after adjusting for PM_{10}. Particulate concentration data were not available for the complete time period of this study, and future studies could determine if PM_{10} would have a similar effect on the strong CO-IHD association.

Studies investigating the relationship between CO and heart failure hospitalizations have consistently reported significant associations.(32, 41, 45, 49) Significant associations were also seen in the current study with the results for these models having some of the largest mean percent changes in risk. Carbon monoxide's negative influence on these cardiovascular conditions may be due to its strong affinity to hemoglobin and myoglobin. It has been reported that individuals with cardiovascular conditions have reduced

amount of myoglobin.(31) Myoglobin and hemoglobin are important oxygen binding proteins. When CO, rather than oxygen, binds to hemoglobin and myoglobin the oxygen-carrying capacity of these proteins within the body is reduced adding additional strain on the heart to pump enough blood to meet the body's needs.(27, 31)

This study found a significant association between the previous day's SO_2 and daily heart failure hospital admissions. A past Canadian study also found a positive association between SO_2 and heart failure hospitalizations for those 65 years and older, however once adjusted for other pollutants (CO, NO_2, O_3 and coefficient of haze) the regression coefficient was near zero.(32) However, the authors did note that results varied greatly between the 10 cities studied and city-specific results for SO_2 were not presented. Other studies have reported non-significant associations.(41, 45, 57) It is unclear why the present study's results are inconsistent with other studies. The major differences with this study are the long study period and low pollutant concentrations. The daily mean SO_2 concentration in Detroit over the 3 year study period was 25.4 ppb while the daily mean SO_2 over the 13 year study period in Vancouver was only 4.85 ppb.(41)

The lone statistically significant association between gaseous pollutants and deaths was found between mean NO_2 concentrations based on same day and previous day's levels and stroke. There have been few similar studies. Kan et al. reported a significant single-pollutant association between previous day's NO_2 exposure and stroke deaths, but when adjusted for other study pollutants (PM_{10} and SO_2) the association was non-significant.(54) The inconsistency in the results may be due to the difference in age

groups of the two studies and the difference in covariates. The present study was focused on those 65 years and older while Kan et al.'s study encompassed the entire Shanghai population and included PM_{10} adjustments. Another study reported an association between stroke deaths and same day O_3 and NO_2, SO_2 and CO in the 2-day lag model, however multiple-pollutant model results were not reported.(52)

In air pollution and morbidity and mortality studies, statistically significant negative results have been rarely reported.(65, 71, 88, 107) Results from the NMMAPS investigation reported negative, non-significant estimates for ozone in association with total mortality, however the study did not model overall or specific cardiovascular conditions.(88) In this study, statistically significant negative results were seen in the associations between NO_2 and daily stroke hospitalizations and O_3 and AMI admissions. The reason for the negative associations remains unclear. In the case of NO_2 and daily stroke hospitalizations, the significant association between NO_2 and daily stroke deaths may have impacted the availability of the susceptible population. If those who are at risk for stroke hospitalization succumb to stroke deaths, the number of susceptible individuals requiring a hospital admission will be reduced. The negative estimates may also be due to unmeasured confounding variables influencing the relationship or inadequate adjustment for time or seasonal trends.

It would have been preferable to include adjustments for particulates in this study however daily PM concentration levels were unavailable for the complete study period. Dichotomous PM data were available for about every sixth day (under 1,000 days out of the over 5,000 study days) and daily tapered-element oscillating microbalance (TEOM)

data were available from January 1, 1994 (PM_{10}) and June 1, 1995 ($PM_{2.5}$). Given the loss of power associated with less study days if the dichotomous PM data were used, this thesis included sensitivity analyses of a truncated study period with TEOM PM adjustments. The results of the sensitivity analyses suggests that further investigation with the inclusion of $PM_{2.5}$ may be of interest but that the addition of PM_{10} has little influence on the association between gaseous air pollutants and cardiovascular hospitalizations or deaths. Although the effects of particulate pollution were not comprehensively investigated in this study, a Canadian study has suggested that CO, NO_2, SO_2 and O_3 can adequately explain daily variations in mortality rates and that $PM_{2.5}$ is unlikely to improve the predictive power of risk estimates.(35)

It is challenging to compare this study's results with other published studies due to variations in model design and outcomes investigated. Reported inconsistent results may be due to uncontrolled confounding or over filtering. Over filtering removes variation in the data, reducing the sample size and in turn reducing the power of the study. If cumulative exposure to air pollution is necessary to produce a morbidity or mortality effect, over filtering may eliminate the effects under investigation.(108) Inconsistencies may also be due to low numbers of morbidity and mortality or low air pollution concentrations. This is consistent with the results of this study. There were far fewer numbers of deaths compared to hospitalizations over the study period and significant associations were more often observed with hospitalizations than with mortality. The power of the study is partially determined by the number of events, in other words the number of hospitalizations or deaths. The smaller number of deaths means the study will have lower power to detect an association even if the association

exists. Results of a Netherlands study reported significant results for those diagnoses with larger numbers of daily hospital admissions and when comparing results between two cities, the city with the higher levels of pollutants showed the more consistent results.(107) This suggests that one model or one lag period may not adequately describe pollutant and outcome associations for studies with low numbers of outcome events and low pollutant concentrations.

Inconsistencies have even been found within investigations. One group of researchers investigated air pollution and hospital admissions in Hong Kong and London and although they concluded that air pollution has harmful health effects, results between the two cities were sometimes vastly different. There were positive associations between cardiac admissions and O_3 in Hong Kong, whereas in London the results showed a negative association. Investigating the dose-response curve of ozone and cardiovascular admissions, the researchers reported a negative linear association for ozone in London and a "J"-shaped curve in Hong Kong showing a positive association between ozone and cardiac admission at the higher concentrations of ozone.(65) A multi-city Canadian study investigating the increased risk of mortality due to air pollution found variation in how pollutants contributed to the risk of mortality between both cities and regions.(35)

Previous studies have reported significant associations between ozone and cardiovascular conditions during the warm season,(42, 69) however results in this study were non-significant with the exception of significant associations with heart failure hospitalizations and stroke deaths during the cool season. The studies used the same

definition for warm and cool season, however the London study's risk estimates were based on an increase between the 10^{th} and 90^{th} percentile for a change of 31 ppb while this studies' difference between the 10^{th} and 90^{th} percentile was 28 ppb.(42) The Montreal study investigated pollutant levels using a 3-day mean lag while this study utilized maximum 1-hour levels of ozone at same day, previous day and the average between the two days lag periods.(69) Additionally, Vancouver has a generally temperate climate with quite similar ozone levels in the two seasons; 21.59 ppb (SD 8.73) in the cool season and 24.51 (SD 10.95) in the warm season.

The estimates of risk between the gaseous air pollutants and the cardiovascular conditions varied between the three lag models. Significant associations for CO and NO_2 were generally seen for same day or average lag models while the significant association between SO_2 and heart failure was reported when modelled with the previous day's SO_2 levels. Given these differences, it may be inappropriate to estimate pollutant effects using the same lag day or period across the four pollutants and the different cardiovascular conditions. The similarity between CO and NO_2 effects based on same day pollutant concentrations may be due to the strong correlation between CO and NO_2. It is also possible that the mechanism by which SO_2 interacts with the body requires more time than the other pollutants.

The sensitivity analysis of the degrees of freedom utilized to smooth the time component of the models suggest that the NMMAPS time smoothing (7 degrees of freedom per year) may slightly underestimate the effect of gaseous pollutants. Less smoothing may be important for associations close to statistical significance.

The NMMAPS methodology does not include adjustment for holidays; however, this variable has been included in other published studies.(42, 47, 50, 55, 65) A comparison of the results from the two methods suggest that without statutory holidays included in the hospitalizations models, mean percent change estimates may be overestimated. This is likely because individuals have more choice about whether or not they go to the hospital on holidays. However, adjusting for holidays in the mortality time-series models has little influence on the resulting estimates. While it may be appropriate to adjust for holidays in future hospitalizations time-series models, in a comparison of this study's models with and without the holiday adjustment (all results not shown) only one association that was statistically significant without the adjustment for holidays (NO_2 and all cardiovascular hospitalizations) was non-significant when the holiday variable was included in the model.

Given the high correlation between mean temperature and mean dew point temperature ($r = 0.94$), this study investigated time-series models with various weather adjustments. When mortality models used either mean temperature or mean dew point temperature to adjust for weather conditions the relationship between NO_2 and stroke was statistically significant. In comparison, when both variables were used to control for weather the association was not significant.

The results of the sensitivity analyses suggest that the addition or exclusion of covariates may slightly influence the mean percent change estimates however, the assorted adjustments did not generally have over-arching influence on statistical

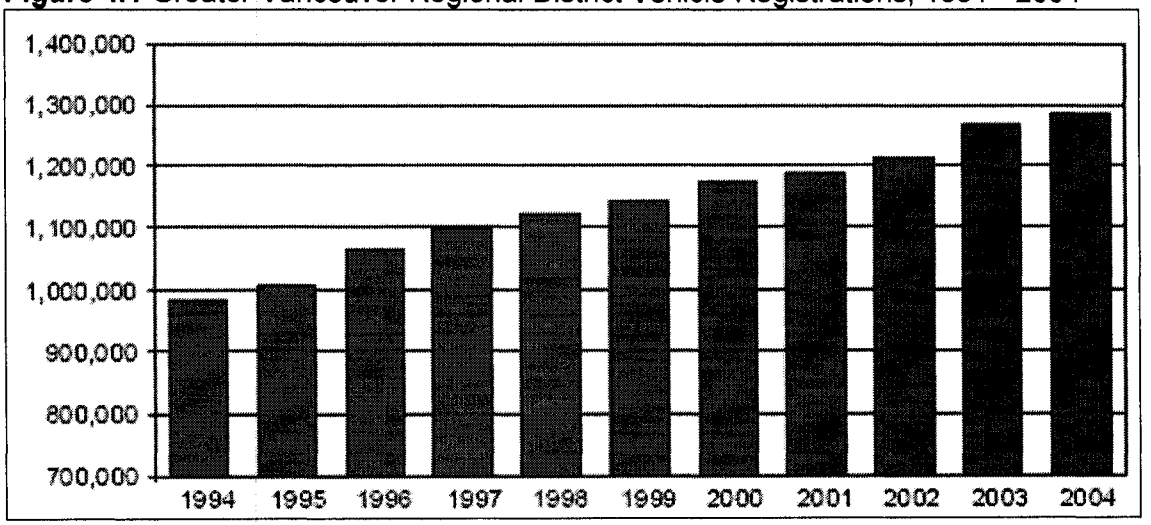
significance of the relationships between gaseous air pollutants and cardiovascular hospitalizations and death.

4.5. Public health importance and implications

The results of the present study suggest that gaseous pollutants are associated with an increase in cardiovascular hospitalizations in the elderly at the relative low pollutant levels found in Vancouver, BC. The population's heath can be expected to benefit from further reductions in ambient air pollution concentrations. In June 2000, the Canadian Council of Ministers of the Environment adopted new lower standards for particulate matter and ozone that commits governments to reach the targets by 2010.(5) Results of this study suggest that the population would further benefit from new lower CO, NO_2 and SO_2 standards.

Vehicle exhaust is a significant contributor to air pollution and accounts for 90% of the CO pollution in Vancouver.(29) Although, between 1996 and 2001, the median distance commuters traveled decreased slightly from 7.7 km to 7.6 km, Figure 4.1 shows the consistently increasing number of vehicles in the Greater Vancouver area.(109)

Figure 4.1 Greater Vancouver Regional District Vehicle Registrations, 1991 - 2004



Source: Insurance Corporation of British Columbia. In: 2004 Annual report on the livable region strategic plan. Greater Vancouver Regional District, 2004.

Programs such as Vancouver's AirCare, that test vehicle emission levels before a vehicle can be re-licensed, and strategies to encourage the use of lower emission fuels, alternate-fuel vehicles or alternative modes of transportation could help to reduce ambient pollutant levels in Vancouver.(110, 111)

5. CHAPTER 5 CONCLUSION

Results of this study suggest that gaseous air pollutants have a negative impact on cardiovascular health at levels below the Canada wide standards for these pollutants. Given these epidemiologic results these objectives should not be viewed as a boundary below which the health of the population is safe, but rather a minimum standard that should be met by communities. Additionally a re-evaluation of the standards may be beneficial.

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