TRAFFIC-RELATED AIR POLLUTION, COMMUNITY NOISE, AND CORONARY HEART DISEASE

by

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Abstract

Cardiovascular disease is the leading cause of death worldwide. Recent evidence suggests associations between exposure to air pollution and community noise and cardiovascular disease mortality. While road traffic is a major common source for air pollution and community noise in urban areas, studies of their joint effects on the risk of cardiovascular disease have been limited.

Linked administrative databases from the British Columbia health insurance system were used to assemble a population-based cohort to investigate the independent and joint effects of traffic-related air pollution and community noise on coronary heart disease (CHD) mortality. The cohort included all residents aged 45-85 years who resided in metropolitan Vancouver, Canada, for at least 5 years at baseline (N~400,000). During a 4-year follow-up period, CHD death cases were identified from the provincial death registration database.

Distances from residences to major roads were first used as a surrogate for exposure to traffic-related pollution. Living close to major roads was associated with CHD mortality and changes in distances to major roads were associated with altered CHD mortality risk in an exposure-response fashion. Both traffic-related air pollution and noise could be responsible for these associations.

Subsequently, land use regression models were used to estimate residential exposure to major traffic-related air pollutants including black carbon, $PM_{2.5}$, NO_2, and NO. Black carbon concentrations were associated with CHD mortality, with a clear exposure-response relationship. No robust associations were found with other air pollutants.

A noise prediction model was then used to estimate annual average community noise levels at each person's residence. Community noise and black carbon were independently associated with CHD mortality: an interquartile range elevation in noise (6.6 dB(A)) and black carbon (0.97×10^{-5}/m) was associated with a 6% (95% CI, 1-11%) and a 4% (95% CI, 1-8%) increase in coronary mortality, respectively. There was no discernable linear exposure-response relationship between community noise and CHD mortality.

Together, these analyses suggest that traffic-related fine particulate air pollution, indicated by black carbon, and traffic noise may both be responsible for observed associations between exposure to road traffic and cardiovascular disease.

Preface

This dissertation includes four mutually dependent original research chapters, each of which has been written as a stand-alone manuscript for publication. Chapters 2 and 3 have been published and Chapter 3 and 4 have been submitted to peer-reviewed journals. The title of each paper, coauthors, and their contributions are specified as follows:

A version of **Chapter 2** has been published. Gan WQ, Tamburic L, Davies HW, Demers PA, Koehoorn M, Brauer M. Changes in residential proximity to road traffic and the risk of death from coronary heart disease. *Epidemiology* 2010; 21(5): 642-649. I designed the study, analyzed and interpreted the data, and wrote the first draft of the manuscript; my overall contribution is over 85%. Michael Brauer initially conceptualized the idea and supervised the data analysis. Lillian Tamburic assembled the residential histories and linked these to exposure estimates. Michael Brauer, Hugh Davies, Mieke Koehoorn, Paul Demers, and Lillian Tamburic assisted in the revision of the manuscript.

A version of **Chapter 3** has been published. Gan WQ, Koehoorn M, Davies HW, Demers PA, Tamburic L, Brauer M. Long-term exposure to traffic-related air pollution and the risk of coronary heart disease hospitalization and mortality. *Environmental Health Perspectives* 2011; 119(4): 501-507. I designed the study, analyzed and interpreted the data, and wrote the first draft of the manuscript. My overall contribution is over 85%. Michael Brauer supervised the study design and data analysis. Lillian Tamburic assembled the residential histories and linked these to exposure estimates. Michael Brauer, Mieke Koehoorn, Hugh Davies, Paul Demers, and Lillian Tamburic assisted in the revision of the manuscript.

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This research was approved by the Institutional Review Board of The University of British Columbia (Behavioural Research Ethics Board certificate # H08-00185).

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List of Abbreviations

ANOVA	One-Way Analysis of Variance
BAQS	Border Air Quality Study
BC	Black Carbon
BMI	Body Mass Index
CAC	Coronary Artery Calcification Score
CHD	Coronary Heart Disease
CI	Confidence Interval
CIMT	Carotid Intima-Media Thickness
CO	Carbon Monoxide
COPD	Chronic Obstructive Pulmonary Disease
dB(A)	A-Weighted Decibels
DVT	Deep Vein Thrombosis
GIS	Geographic Information System
ICD	International Classification of Diseases
IDW	Inverse Distance Weighted
IQR	Interquartile Range
L_{day} dB(A)	Annual Daytime A-Weighted Equivalent Continuous Noise Level
L_{den} dB(A)	Annual Day-Evening-Night A-Weighted Equivalent Continuous Noise Level
L_{eq} dB(A)	A-Weighted Equivalent Continuous Noise Level
L_{night} dB(A)	Annual Nighttime A-Weighted Equivalent Continuous Noise Level

LUR	Land Use Regression
MI	Myocardial Infarction
MSP	Medical Services Plan
NO	Nitric Oxide
NO_2	Nitrogen Dioxide
NO_x	Nitrogen Oxides
OR	Odds Ratio
$PM_{2.5}$	Particulate Matter with Aerodynamic Diameter ≤ 2.5 μm
PM_{10}	Particulate Matter with Aerodynamic Diameter ≤ 10 μm
ROS	Reactive Oxygen Species
RR	Relative Risk
SD	Standard Deviation
SEL	Sound Exposure Level
SES	Socioeconomic Status

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Chapter 1: Introduction

1.1 Literature Review

1.1.1 Traditional Risk Factors for Cardiovascular Disease

Cardiovascular disease (CVD) is the leading cause of death worldwide and is projected to remain the leading cause of death during the next two decades.[1] In 2004, about 17 million people died from various cardiovascular diseases, representing about 30% of total global deaths. Of these cardiovascular deaths, 75% were due to coronary heart disease (CHD) and stroke.[1] In both British Columbia and Canada, cardiovascular deaths account for more than 30% of total deaths; CHD and stroke account for about 70% of total cardiovascular deaths.[2, 3]

Since the 1940s after the Second World War, extensive epidemiologic and experimental studies have identified the major risk factors for cardiovascular diseases (Table 1.1).[4, 5] Except for advancing age, male sex, race, and family history, almost all other cardiovascular risk factors including tobacco smoke, high blood pressure, high blood cholesterol, abdominal obesity, physical inactivity, unhealthy diets, and psychosocial stress can be prevented, treated, and controlled .[6, 7] These lifestyle, dietary, and metabolic risk factors are responsible for the vast majority of cardiovascular hospitalizations and deaths.[8, 9] The understanding of these cardiovascular risk factors has substantially promoted worldwide cardiovascular disease prevention and control, especially in industrialized countries. In the United States, the prevalence of cigarette smoking in adults declined from 42% to 25% during the period 1965 to 1995; average blood pressure, blood cholesterol, physical inactivity, and dietary saturated fat and cholesterol levels declined; hypertension

management and evidence-based cardiovascular disease therapies improved. Corresponding to these progresses, total age-adjusted cardiovascular mortality declined 60% from 1950 to 1996, representing one of the greatest public health achievements in the 20th century.[4, 10]

In recent decades, a growing body of evidence has demonstrated that ambient air pollution, especially particulate matter with an aerodynamic diameter < 2.5μm ($PM_{2.5}$), is associated with increased cardiovascular morbidity and mortality.[11-16] Meanwhile, some epidemiologic studies have also shown that exposure to community noise including road traffic noise and aircraft noise is associated with an increased risk of cardiovascular events.[17-23] Worldwide, air pollution and community noise have been increasingly regarded as important public health problems. [24-27]

1.1.2 Sources of Air Pollution

Air pollution is a complex mixture of particles, gases, and liquids, mainly derived from the combustion of fossil fuels for transportation, heating and cooking, power generation, and industrial processes. Primary air pollutants (e.g. black carbon and carbon monoxide) are emitted directly into the atmosphere, whereas secondary air pollutants (e.g. ozone) are formed in the atmosphere as a result of chemical reactions between primary pollutants and atmospheric components. [12, 26] Some pollutants (e.g. $PM_{2.5}$ and NO_2) are both primary and secondary pollutants, they are emitted directly and formed from other pollutants.[12, 26, 28] Because road traffic is the major source of ambient air pollution in most metropolitan areas,[28] this section focuses on the sources of traffic-related air pollutants

including black carbon, $PM_{2.5}$, nitrogen dioxide (NO_2), nitric oxide (NO), and carbon monoxide (CO).

For primary air pollutants, the ambient concentrations are strongly dependent on emission levels and the distance from the source of the emissions.[28] Black carbon is produced by incomplete combustion of various carbon-containing fuels. It comes mainly from diesel exhaust, but may also be emitted from gasoline-powered vehicles and wood combustion.[29] In metropolitan areas, black carbon may serve as an indicator for traffic-related fine particulate air pollution; [29-31] it is useful in evaluating the effectiveness of traffic control measures in metropolitan areas.[31, 32]

$PM_{2.5}$ is emitted directly from numerous natural (e.g. windblown soil) and anthropogenic (e.g. motor vehicle emissions) sources; it is also produced through physiochemical transformation of gaseous pollutants.[12, 28] Fine particles have long atmospheric lifetimes and can be dispersed over large areas; therefore, the spatial distribution of $PM_{2.5}$ is relatively homogeneous over a metropolitan area.

Nitrogen oxides (NO_x) including NO and NO_2 originate mostly from high-temperature combustion of fossil fuel in motor vehicles and industrial process such as power generation. Almost all NO_x is emitted as NO, which is then rapidly oxidized to NO_2 in the atmosphere.[12, 26] When NO_2 is exposed to the ultraviolet radiation in sunlight, it splits into NO and a single atom of oxygen (O), which quickly combines with oxygen (O_2) to produce ozone (O_3). The ozone molecule rapidly reacts with NO to produce NO_2.[12, 33] Although a small amount (5%) of NO_2 is emitted as a primary pollutant, the major proportion of NO_2 is produced in the atmosphere as a secondary product.[26] On warm and

sunny days, especially during the summer time, O_3 is typically produced in greater amounts and the concentrations may continue to rise all day long and then rapidly decrease after sunset. NO_x also contributes to the formation of ambient $PM_{2.5}$ as a result of oxidation to form nitrate aerosols.[12, 28] NO_2 is one of the regulated air pollutants, and correlated with other traffic-related air pollutants;[34] it is thus often used as a surrogate for traffic-related air pollution in epidemiologic studies.[35, 36]

CO is a product of incomplete combustion of carbon-containing fuels. Internal combustion engines such as motor vehicles and motorboats are the main sources of CO.[12, 28] In metropolitan areas, the contribution of road traffic ranges from 62% to nearly 100%.[28]

1.1.3 Air Pollution Exposure Assessment

Accurate exposure assessment is critical in epidemiologic studies to identify the associations of air pollutants with adverse health effects and quantify the magnitudes of the adverse effects. Although personal continuous monitoring during an entire study period may be regarded as the gold standard for exposure assessment, in practice this approach is often not feasible because of financial and logistical restrictions.[37] This is particularly true for large-scale long-term epidemiologic studies. This section briefly introduces some air pollution exposure assessment methods that are widely used in epidemiologic studies. Published comprehensive reviews provide more detailed discussions on this topic.[37-39]

In most metropolitan areas, regulatory air quality monitoring networks routinely perform continuous measurements of some regulated air pollutants. In epidemiologic studies, the monitoring data may be assigned to study participants using the nearest

monitor or inverse-distance weighted (IDW) interpolation approaches.[40] This data source can accurately reflect the temporal variability of urban background concentrations of air pollutants and has been widely used in time-series studies to investigate the relationships between temporal variability of air pollution and the risk of acute events such as daily mortality and hospital admission.[15, 41] However, because few such monitors are distributed in a large region, the monitoring data generally cannot reflect the spatial variability of air pollution in metropolitan areas. This limitation hinders the use of these data in intra-urban epidemiologic studies.[37]

Land use regression (LUR) modeling uses a quantitative relationship established between land use characteristics (e.g. distance from major road, traffic density, population density, and surrounding land use characteristics) and the concentrations of an air pollutant measured at multiple representative locations in a region to predict the concentrations of the pollutant across the entire region in a Geographic Information System (GIS).[42-44] Compared with air quality monitoring data, the major advantage of LUR modeling is that it can describe detailed spatial variability of air pollutants in a study region (e.g. 10 m spatial resolution).[37, 38] The modeling data are particularly useful in estimating residential exposure to traffic-related air pollution. Importantly, LUR models can be used in combination with regulatory monitoring data to describe both spatial variability and long-term temporal variability of air pollution levels in a study region.[37, 40]

Dispersion models are based on the Gaussian plume dispersion equation to estimate or predict the concentrations of air pollutants emitted from various sources such as road traffic or industrial facilities. This modeling is performed by using detailed input data on

pollution emissions, meteorological and topographical conditions, and land use characteristics.[45] Dispersion models are able to estimate the potential impacts of changes in pollution sources (e.g. new facilities) and simulate air pollution episodes. Dispersion models can potentially incorporate both spatial and temporal variability of air pollution in a study region. The major disadvantages of using dispersion models in epidemiologic studies are the requirements for intensive data input that may not be readily available and the complex modeling processes that may be expensive and time-consuming.[37, 38] Recent studies have shown that dispersion and LUR models could complement each other, combining these different models could take advantage of existing data sources and improve the accuracy of exposure assessment.[46-48]

It should be noted that these exposure assessment methods can only estimate exposure levels outside the residences of participants, they cannot precisely reflect actual individual exposure levels,[49] because some factors such as indoor air pollution,[50] indoor infiltration of outdoor pollution,[51] individual mobility,[52] and occupational exposure might substantially affect actual individual exposure.

1.1.4 Air Pollution and Cardiovascular Disease

The World Health Organization estimates that air pollution causes approximately 2 million premature deaths worldwide each year.[24] Although many air pollutants may cause adverse health effects individually or in combination, PM including $PM_{2.5}$ and PM_{10} has become a major focus of epidemiologic studies because PM is a strong indicator of ambient air pollution and more consistently associated with adverse health effects, in

particular cardiovascular and respiratory morbidity and mortality.[11, 12] A recent American Heart Association scientific statement provided a comprehensive literature review on the relationships between PM exposure and cardiovascular disease, and concluded that short-term (e.g. hours to weeks) exposure to $PM_{2.5}$ may trigger fatal and non-fatal cardiovascular events, and that long-term (e.g. years) exposure to $PM_{2.5}$ may increase cardiovascular mortality to an even greater extent than short-term exposures.[11]

Air pollution exposures can be divided into short-term exposures and long-term exposures. For short-term exposures, time-series studies (Poisson regression) are generally used to investigate the relationships between daily variation of air pollutant concentrations and changes in cardiovascular events after controlling for seasonal and temporal variability. For long-term exposures, cohort studies (Cox regression) are generally used to investigate the relationships between city-specific or individual-specific average concentrations of air pollutants during a specific period and the risk of cardiovascular events after adjusting for individual cardiovascular risk factors. Short-term exposure studies reflect the acute adverse effects of air pollution, whereas long-term exposure studies reflect the accumulation of both acute and chronic adverse effects of air pollution. Therefore, long-term exposure studies typically yield larger effect estimates than short-term exposure studies.[53, 54]

1.1.4.1 Epidemiologic Studies of Short-Term Exposure to Air Pollution and Cardiovascular Events

There are numerous epidemiologic studies on the associations of short-term exposures to air pollution with cardiovascular mortality and hospitalization, as reviewed in the 2004 and 2010 American Heart Association scientific statement.[11, 12] The following is a brief introduction of major short-term exposure studies on cardiovascular mortality and hospitalization.

1.1.4.1.1 Cardiovascular Mortality

Two large short-term exposure studies have examined the associations of air pollution with total and cause-specific mortality: the National Mortality and Morbidity Air Pollution Study (NMMAPS) in the US and the Air Pollution and Health: a European Approach (APHEA-2) in Europe.[15, 55] The NMMAPS was conducted in the 20 largest cities with 50 million participants from 1987 to 1994. The study found that each 10 $\mu g/m^3$ elevation in daily PM_{10} concentrations (range of city-specific daily mean, 23.8-46.0 $\mu g/m^3$) was associated with a 0.21% ($\pm$0.06 SE) and a 0.31% ($\pm$0.09 SE) increase in daily all-cause and cardiopulmonary mortality, respectively.[15] The APHEA-2 study was conducted in 29 European cities with 43 million participants for more than 5 years in 1990s. The study found that each 10 $\mu g/m^3$ elevation in daily PM_{10} concentrations (range of city-specific daily mean, 15.5-76.2 $\mu g/m^3$) was associated with a 0.6% (95% CI, 0.4-0.8%)[55] and a 0.69% (95% CI, 0.31-1.08%)[56] increase in daily all-cause and cardiovascular mortality, respectively.

1.1.4.1.2 Cardiovascular Hospitalization

The APHEA-2 hospitalization study found that each 10 μg/m^3 elevation in daily PM_{10} and black smoke (range of city-specific daily mean, 13.1-55.7 μg/m^3) concentrations was respectively associated with a 0.5% (95% CI, 0.2-0.8%) and a 1.1% (95% CI, 0.4-1.8%) increase in daily cardiovascular hospitalizations as well as a 0.8% (95% CI, 0.3-1.2%) and a 1.1% (95% CI, 0.7-1.5%) increase in daily CHD hospitalizations for participants aged 65 years and old.[57]

A large time-series study conducted in 204 US urban counties with 11.5 million Medicare participants ≥ 65 years found that daily variation in $PM_{2.5}$ concentrations was associated with daily hospitalizations for CHD, stroke, heart failure, and heart rhythm disturbance.[13] Chemical components of $PM_{2.5}$ including elemental carbon, vanadium, and nickel might be responsible for the association.[58] Similarly, Peng et al examined emergency hospitalizations for cardiovascular disease associated with seven major chemical components in $PM_{2.5}$ and found that an interquartile range (IQR) elevation in daily elemental carbon concentrations (median, 0.58 μg/m^3; IQR, 0.40 μg/m^3) was associated with a 0.80% (95% CI, 0.34-1.27%) increase in same-day cardiovascular hospitalizations. Elemental carbon was the only component that was significantly associated with cardiovascular hospitalizations.[41]

A 6-year time series study in Ontario, Canada found that each 13 μg/m^3 increase in daily particulate sulfate concentrations (range of daily mean, 2.0-7.7 μg/m^3) was associated with a 2.8% (95% CI, 1.8-3.8%) increase in next day hospital admissions for cardiovascular diseases including CHD, cardiac dysrhythmias, and heart failure.[59] A meta-

analysis of hospital admission studies showed that each 10 μg/m^3 elevation in daily PM_{10} concentrations was associated with a 0.8% (95% CI, 0.5-1.2%), 0.7% (95% CI, 0.4-1.0%), and 0.2% (95% CI, -0.2 to 0.6%) increase in daily hospital admissions for congestive heart failure (4 studies, time lag 0-2 days), CHD (5 studies, time lag 0-3 days), and stroke (5 studies, time lag 0-1 day), respectively.[60]

Exposure to road traffic signifies exposure to traffic-related air pollution and traffic noise.[61, 62] A case-crossover study of 691participants who had survived for ≥ 24 hours after the onset of myocardial infarction (MI) in Augsburg, Germany found that exposure to road traffic was associated with an increase by a factor of 2.92 (95% CI, 2.22-3.83) in the risk of MI within one hour. Various traffic exposures including cars, public transportation, motorcycles, or bicycles were consistently associated with the risk of MI.[63]

For those with preexisting cardiovascular conditions, short-term exposure to elevated PM concentrations was also associated with an increased risk of hospital admissions for cardiovascular diseases including CHD[64]and congestive heart failure.[65] For example, a case-crossover study of 12,865 patients with cardiac catheterization in Utah found that each 10 μg/m^3 increase in daily $PM_{2.5}$ concentrations was associated with a 4.5% (95% CI, 1.1-8.0%) increase in same-day acute ischemic coronary events including unstable angina and MI, especially among those with underlying CHD.[64] Another case-crossover study of 22,006 survivors of a first MI in five European cities during 1992-2001 demonstrated that daily cardiac hospital readmission was associated with same-day PM_{10} and NO_2 concentrations, respectively.[66]

In summary, numerous epidemiologic studies have demonstrated that short-term exposure to elevated concentrations of air pollutants including $PM_{2.5}$,[13, 64] PM_{10},[15, 55-57, 60, 65, 66] elemental carbon,[41, 58] NO_2,[66] and road traffic[63] is associated with increased hospitalizations[13, 57, 59, 63-66] and mortality[15, 55, 56] due to cardiovascular diseases including CHD[13, 59, 60, 63, 64, 66] stroke,[13, 60, 66] congestive heart failure,[13, 59, 60, 65, 66] and cardiac dysrhythmias.[13, 59, 66]

1.1.4.2 Epidemiologic Studies of Long-Term Exposure to Air Pollution and Cardiovascular Events

This dissertation is based on population-based cohort studies, therefore a detailed review of cohort studies and some influential cross-sectional studies on the associations between air pollution and cardiovascular disease is provided below.

The Harvard Six Cities Study is the first cohort study of ambient air pollution and adverse health outcomes.[67] The study followed 8111 adults in six US cities for 14 to 16 years and found that when $PM_{2.5}$ (range of city-specific mean, 11.0-29.6 $\mu g/m^3$) was used as the indicator of ambient air pollution, for residents who lived in the most-polluted city, the all-cause and cardiopulmonary mortality increased 26% (95% CI, 8-47%) and 37% (95% CI, 11-68%), respectively, compared with those who lived in the least-polluted city after adjusting for age, sex, body mass index (BMI), and smoking status. When PM_{10} (range of city-specific mean, 18.2-46.5 $\mu g/m^3$) or sulfate particles (range of city-specific mean, 4.8-12.8 $\mu g/m^3$) was used as the indicator of air pollution, the results were similar.[67] After extended follow-up during a period of air pollution reduction, the study found that

adjusted mortality declined from period 1, 1974-1989 (range of city-specific mean $PM_{2.5}$, 11.4-29.0 $\mu g/m^3$) to period 2, 1990-1998 (range of city-specific mean $PM_{2.5}$, 10.2-22.0 $\mu g/m^3$). The decline in adjusted mortality rate was the largest for the city with the largest reduction in $PM_{2.5}$ concentrations. Overall, a 10 $\mu g/m^3$ decrease in $PM_{2.5}$ concentrations was associated with a 27% (RR, 0.73; 95% CI, 0.57-0.95) reduction in all-cause mortality and a 31% (RR, 0.69; 95% CI, 0.46-1.01) reduction in cardiovascular mortality.[68] This study has demonstrated that long-term exposure to fine-particulate air pollution contributes to excess all-cause and cardiopulmonary mortality; whereas the improvement of air quality can reduce these adverse health effects.[67, 68]

The American Cancer Society's (ACS) Cancer Prevention Study II (CPS-II) is so far the largest cohort study in this area.[16, 69, 70] This study followed 500,000 adults in all 50 states for 16 years and found that each 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentrations (city-specific mean, 17.1 $\mu g/m^3$; SD, 3.7 $\mu g/m^3$) was associated with a 6% (95% CI, 2-11%) and a 9% (95% CI, 3-16%) increase in all-cause and cardiopulmonary mortality, respectively, after adjusting for age, sex, race, BMI, smoking status, education, marital status, alcohol consumption, diet, and occupational exposure.[16] The observed association was linear and without a discernible threshold.[16] Importantly, this study found that the largest increase in mortality was from CHD (RR, 1.18; 95% CI, 1.14-1.23); the mortality from arrhythmia, heart failure, and cardiac arrest was also significantly increased (RR, 1.13; 95% CI, 1.05-1.21).[70] These findings indicate that possible mechanisms underlying the observed associations include pulmonary and systemic inflammation, accelerated atherosclerosis, and over-activated cardiac autonomic function.[70]

Recently, the Women's Health Initiative Observational Study (WHI) followed 65,893 postmenopausal women without previous cardiovascular disease in 36 American metropolitan areas for about 6 years.[14] Individual exposure to air pollutants were measured using a monitor close to each woman's residence (within 48 km). The annual (year 2000) $PM_{2.5}$ concentrations varied from 3.4 to 28.3 $\mu g/m^3$ (mean, 13.5 $\mu g/m^3$) across the study areas. The study found that for each 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentrations, the overall risk (including between-city and within-city effects) increased 24% (95% CI, 9-41%) for cardiovascular events, 21% (95% CI, 4-42%) for coronary events; the mortality increased 76% (95% CI, 25-147%) for cardiovascular disease, 121% (95% CI, 17-316%) for CHD after adjusting for age, race, education, smoking status, household income, systolic blood pressure, BMI, diabetes, hypertension, and hypercholesterolemia.[14]

In most previous studies, average concentrations of air pollutants across a metropolitan area were assigned to all participants in this area.[16, 67-70] This exposure assessment method may have resulted in severe exposure misclassification because actual individual exposure levels may vary substantially across a metropolitan area. For example, individuals living in city centers or near major roads may experience higher levels of exposure to air pollution.[43, 71] Exposure misclassification may theoretically bias effect estimates toward the null. The WHI Study compared the effect estimates based on within-city and between-city exposure assessment and found that within-city effect estimates tend to be larger than between-city effect estimates (e.g. each 10 $\mu g/m^3$ increase in $PM_{2.5}$, RR, 2.28; 95% CI, 1.10-4.75 versus RR, 1.63; 95% CI, 1.10-2.40 for cardiovascular mortality);[14] including within-city exposure assessment resulted in substantially higher risk

estimates (e.g. overall RR, 1.76; 95% CI, 1.25-2.47 for cardiovascular mortality)[14] compared with those of previous studies.[16, 67-70] Similarly, in a subgroup analysis of the ACS-CPS-II Study using the Los Angeles dataset,[72] Jerrett et al found that within-city effect estimates were greater than between-city effect estimates (e.g. each 10 $\mu g/m^3$ increase in $PM_{2.5}$, RR, 1.39; 95% CI, 1.12-1.73[72] versus RR, 1.18; 95% CI, 1.14-1.23[70] for CHD mortality). However, this situation was not observed in another subgroup analysis using the New York dataset.[73]

The Netherlands Cohort Study on Diet and Cancer (NLCS) is the first relevant study conducted in Europe,[74] where air pollution was generally more severe than that in the US.[75] This study followed 120,852 participants aged 55-69 years who lived in 204 municipalities across the country from 1987 to 1996. To take into account small-scale spatial variation in air pollutant concentrations, each participant's exposure at home address was evaluated by combining regional exposure (IDW interpolation of air quality monitoring data), urban exposure (population density and land use characteristics), and local exposure (road network and traffic density around each residential address).[76] This study found that each 10 $\mu g/m^3$ increase in $PM_{2.5}$ (mean, 28.3 $\mu g/m^3$; range, 23.0-36.8 $\mu g/m^3$) and black smoke concentrations (mean, 16.5 $\mu g/m^3$; range, 8.7-35.8 $\mu g/m^3$) was associated with a 4% (95% CI, -10 to 21%) and a 4% (95% CI, -5 to 13%) increase in cardiovascular mortality, respectively, after adjustment for age, sex, smoking status, and area indicator of socioeconomic status (SES).[74] It is unknown why adverse cardiovascular effect estimates are not consistent across different studies; it may be due to the differences

in air pollutant concentration and composition, exposure assessment methods, meteorological conditions, and demographic characteristics.[12]

A subgroup analysis of a random sample of 5,000 participants from the NLCS Study found that living near a major road (within 100 m of a freeway or 50 m of a major road) was associated with increased cardiopulmonary mortality (RR, 1.95; 95% CI, 1.09-3.52) after adjustment for age, sex, BMI, education, occupation, active and passive cigarette smoking, and neighborhood SES.[77] Likewise, a 13-year cohort study of 4,800 women aged 50-59 years in North Rhine-Westphalia, Germany also found that living within 50 m of a major road was associated with increased cardiopulmonary mortality (RR, 1.70; 95% CI, 1.02-2.81).[78] These studies have indicated that living near a major road may serve as a convenient surrogate for residential exposure to traffic-related air pollution.

Recently, a large cohort study including all Rome residents aged 35-84 years during 1998-2000 found that a 10 $\mu g/m^3$ increase in residential NO_2 concentrations (range of annual mean, 24-73 $\mu g/m^3$) was associated with a 3% (95% CI, 0-7%) increase in the risk of fatal and non-fatal coronary events and a 7% (95% CI, 2-12%) increase in the risk of fatal coronary events after adjustment for age, sex, and neighborhood SES.[36] Interestingly, this study did not find associations between residential NO_2 concentrations and hospital readmission or mortality for those who survived the first coronary events.[36] Similarly, a cohort study in Oslo, Norway followed 16,209 men aged 40-49 years for five year (1974-1978) and found that a 10 $\mu g/m^3$ increase in residential nitrogen oxides (NO_x) concentrations (median of 5-year mean, 10.7 $\mu g/m^3$; range, 0.7-168.3 $\mu g/m^3$) was associated with a 8% (95% CI, 3-12%) increase in CHD mortality and a 4% (95% CI, -6 to

15%) increase in stroke mortality after adjustment for age, smoking status, education, occupation, physical activity, and the history of cardiovascular disease.[79] These studies have shown that exposure to NO_2 or NO_x, as an indicator of traffic-related air pollution, is associated with adverse cardiovascular outcomes.

A 5-year small-area level ecological study used 1030 census enumeration districts in Sheffield, UK as the unit of analysis. This study found that stroke mortality was 37% (95% CI, 19-57%), 33% (95% CI, 14-56%), and 26% (95% CI, 10-46%) higher in the area with the highest (quintile 5) NO_x (range, 47.6-61.9 $\mu g/m^3$), PM_{10} (range, 16.0-23.3 $\mu g/m^3$), and CO (range, 360-482 $\mu g/m^3$) concentrations, respectively, compared with the area with the lowest (quintile 1) pollutant concentrations. Corresponding increase in stroke hospitalization was 13% (95% CI, 1-27%), 13% (95% CI, -1 to 29%), and 11% (95% CI, -1 to 25%) for NO_x, PM_{10}, and CO, respectively.[80] Another study with the same study design including 113,465 census enumeration districts in England and Wales found that stroke mortality was 7% (95% CI, 4-9%) higher for men $\geq$ 45 years who lived within 200 m (enumeration district centroid) from a major road compared with those who lived at least 10,000 m away from a major road. The corresponding increase was 4% (95% CI, 2-6%) for women and 5% (95% CI, 4-7%) for men and women combined.[81]

Atherosclerosis is a term used to describe the thickening and hardening of arteries, it is the pathological foundation for various CHD.[82] When fat, cholesterol, calcium, and other substances build up within the inner lining of coronary arteries, the arteries become hardened and narrowed.[82] The supply of blood with oxygen and nutrients to myocardial cells is thus substantially reduced, leading to heart attack or other CHD. The severity of

atherosclerosis may be estimated using the coronary artery calcification (CAC) score and the carotid intima-media thickness (CIMT).[83, 84] Because these measurements can objectively reflect the progress of atherosclerosis in arteries, they are thus regarded as better disease evidence compared with subjective disease diagnoses. A cross-sectional study of 4494 participants aged 45-74 years without prior CHD in the Ruhr area of Germany found that compared with participants who lived more than 200 m away from a major road, those who lived within 50 m, 51-100 m, and 101-200 m from a major road had a RR of 1.63 (95% CI, 1.14-2.33), 1.34 (95% CI, 1.00-1.79), and 1.08 (95% CI, 0.85-1.39), respectively, for an elevated CAC score (above the age-and gender-specific 75th percentile). Quantitatively, a reduction in the distance between a residence and a major road by half was associated with a 7.0% (95% CI, 0.1-14.4%) increase in CAC score after adjusting for $PM_{2.5}$ and other relevant factors including age, sex, education, passive and active smoking status, physical inactivity, waist-to-hip ratio, diabetes, blood pressure, blood lipids, city and area of residence.[83] Another earlier cross-sectional study of 798 participants about 59 years of age with increased risk of cardiovascular disease (indicated by elevated blood LDL cholesterol or homocysteine) in Los Angeles found that for a $10\,\mu g/m^3$ increase in $PM_{2.5}$ concentrations (annual mean, $20.3\,\mu g/m^3$; range, 5.2-26.9 $\mu g/m^3$), the CIMT increased by 5.9% (95% CI, 1-11%). The association was stronger for the elderly ($\geq$ 60 years), women, never smokers, and those receiving lipid-lowering therapy.[84] These studies provide direct evidence that long-term exposure to traffic-related air pollution and $PM_{2.5}$ was associated with the severity of artery atherosclerosis.[83, 84]

Prothrombin time (PT) is a test to measure the function of blood coagulation. Lower PT suggests a hypercoagulable status, where blood clots more quickly than usual. A case-control study of 870 cases with deep vein thrombosis (DVT) and 1210 healthy controls in Lombardy, Italy found that the mean PM_{10} concentrations in the year before the diagnosis of DVT for cases or before the examination for controls (range, 12.0-51.5 $\mu g/m^3$) was inversely associated with shortened PT in both DVT cases (β = -0.12; 95% CI, -0.23 to 0.00) and healthy controls (β = -0.06; 95% CI, -0.11 to 0.00). Each 10 $\mu g/m^3$ increase in PM_{10} concentrations was associated with a 70% (95% CI, 30-123%) increase in DVT incidence after adjusting for major cardiovascular disease risk factors.[85] The findings that long-term exposure to particulate air pollution was associated with enhanced prothrombotic status and an increased risk of DVT suggest that activated blood coagulation and thrombosis may be partly responsible for the associations between air pollution and cardiovascular events.

In summary, strong evidence has demonstrated that long-term exposure to air pollution is associated with increased cardiovascular morbidity[14, 36, 74, 84, 85] and mortality[14, 16, 36, 67-70, 74, 77-81] including CHD,[14, 36, 70, 72, 79] stroke,[14, 79-81] dysrhythmias, [70] heart failure,[70] cardiac arrest,[70] and severe artery atherosclerosis.[83-85] Among various air pollutants, PM including $PM_{2.5}$,[14, 16, 67-70 74, 84] PM_{10},[67, 74, 80, 85] black smoke,[74, 77] and sulfate particles[16, 67, 69, 70] is a strong indicator of ambient air pollution. In addition, living near a major road,[77, 78, 81, 83] NO_2,[36, 78] and NO_x,[79, 80] as indicators of traffic-related air pollution, are also associated with cardiovascular morbidity and mortality (Table 1.2).

1.1.5 Acoustical Measurements

In the atmosphere, sound is transmitted by a series of pressure variations from its source to the surroundings, and sound pressure is measured using a microphone. Because the range of sound pressure is very large (10^{-5} to 10^{2} Pa), the direct measurement of sound pressure would lead to large and unwieldy numbers. Therefore, in practice, a convenient scale, sound pressure level (L_p, decibel) is used for acoustical measurements.[86]

($L_p = 10\log_{10}\left(\frac{p}{p_0}\right)^2$, where p is the sound pressure being measured, p_0 is the reference sound pressure, 2×10^{-5} Pa). The audible range of human hearing is 0 to 120 dB, with zero as the minimum threshold of human hearing and 120 dB as the approximate threshold of pain. Because sound pressure levels are measured on a logarithmic scale, they should be added logarithmically, not arithmetically ($L_T = 10\log_{10}\left[\sum_{i=1}^{n} 10^{L_i/10}\right]$, where L_i represents the i^{th} sound pressure level, L_T is the combined total sound pressure level).[25, 86]

Most environmental sounds are a complex mixture of many different frequencies. The audible frequency range is roughly from 20 Hz to 20 kHz, but human hearing is more sensitive to sounds in the frequency range about 2-5 kHz. To reflect the differential sensitivity of human hearing to sounds of different frequencies, the A-weighting is most commonly used to weight mid-and higher-frequencies as more important than lower frequencies. This is called the A-weighted sound pressure level (dB(A)).[25]

The sound pressure levels of most community noise sources fluctuate substantially with time. When sound pressure levels are measured, the instantaneous sound pressure fluctuations should be integrated over a specific time interval. Therefore, equivalent

continuous sound pressure level (L_{eq}) is widely used for measurements; it represents the continuous steady sound pressure level which contains the same total acoustic energy as the measured time-varying sound pressure level over a given time period. Because L_{eq} measures the energy content of a sound over a specific time period, sounds with different characteristics (e.g. continuous and impulse noise) may have the same L_{eq} level. L_{eq} is a good metric for continuous noise such as road traffic noise, but it is not appropriate for high-level discrete noise such as aircraft noise.[25, 86] Instead, A-weighted sound exposure level (SEL) may be used to evaluate discrete noise. SEL is the total noise energy produced from a single noise event such as an individual aircraft flyover.[25]

Based on L_{eq}, an integrated annual average noise metric, day-evening-night equivalent sound pressure level (L_{den}) calculated for an annual period has been widely used for model-based population noise exposure assessment. To reflect increased sensitivity of residents to community noise at evening and night, a 5 dB(A) weighting is added to evening noise levels and a 10 dB(A) weighting to night noise levels.[87]

$$L_{den} = 10 \times \log \frac{1}{24} \times (Time_{day} \times 10^{L_{day}/10} + Time_{evening} \times 10^{(L_{evening}+5)/10} + Time_{night} \times 10^{(L_{night}+10)/10}),$$

where L_{day}, $L_{evening}$, and L_{night} represent the A-weighted daytime, evening time, and nighttime equivalent continuous sound pressure level, respectively.

1.1.6 Noise Source and Exposure Assessment

There is no distinction between sound and noise in physics, noise is usually defined as unwanted sound. Noise is one of the most ubiquitous environmental pollutants worldwide, especially in industrialized countries.[25] Community noise is mainly produced

from transportation (road traffic, railway, and aircraft), surrounding industries (e.g. construction equipment), building service (e.g. ventilation and air conditioning), domestic noise (e.g. vacuum cleaners and lawn mowers), and leisure activities (e.g. loud music, outdoor parties, and motor racing).[25] Among these noise sources, transportation noise, particularly road traffic noise, is the major source of community noise pollution in most metropolitan areas.[25, 88]

Road traffic noise is mainly generated from the engine and frictional interaction between the tires and the ground.[88] Larger and heavier vehicles generally produce more noise than smaller and lighter vehicles. Vehicle speed is another important factor that determines noise emission levels: when the speed is less than 20 km/h, noise emission levels are lower and the engine is the major noise source; when the speed is over 50 km/h, noise emission levels are higher and tire-road interaction is the dominant source of noise.[88] Road traffic noise levels can be predicted from vehicle speed, traffic volume, traffic composition (e.g. the proportion of heavy trucks), and road type and surface. Further, road traffic operating conditions (e.g. traffic lights and intersections), topographical and meteorological conditions may substantially influence traffic noise emissions levels.[25, 88] In addition, aircraft and railway noise sources may affect populations living in the surrounding areas. Aircraft can produce substantial noise during takeoffs and landings while railway noise levels depend mainly on the speed of the train.[25]

Like air pollution exposure assessment, personal noise exposure monitoring is not feasible in community noise epidemiologic studies because of financial and logistical restrictions. Instead, noise prediction models are widely used to estimate residential

exposure to community noise through quantitative analyses of the generation, propagation, and attenuation of various noise sources. [21-23, 87, 89] Chapter 4 provides a detailed analysis of model-based community noise exposure assessment in metropolitan Vancouver.

1.1.7 Noise Exposure and Cardiovascular Disease

It has been well documented that noise exposure may cause annoyance, sleep disturbance, communication interference, and psychological effects (headache, fatigue, irritability).[25, 27] More importantly, recent evidence has indicated that long-term exposure to excessive noise is associated with increased risk of cardiovascular events including CHD and hypertension.[17-20] The following is a review of epidemiologic studies on the associations between exposure to community or occupational noise and cardiovascular diseases.

1.1.7.1 Cohort Studies

The Hypertension and Exposure to Noise near Airports Study (HYENA) was designed to investigate the associations between exposure to aircraft and road traffic noise and the risk of hypertension.[19] This retrospective cohort study included 4861 subjects aged 45-70 years who lived at least 5 years near six major European airports. The study found that a 10 dB(A) increase in residential nighttime aircraft noise levels and daily road traffic noise levels was associated with a 14% (95% CI, 1-29%) and a 10% (95% CI, 0-20%) increase in the incidence of hypertension, respectively, after adjusting for age, sex, BMI, alcohol intake, country, education, and physical exercise. In this study, cigarette smoking

did not significantly affect the observed associations and thus was not included in the analysis.[19] In a 10-year cohort study with 2027 male participants (half of the participants had a family history of diabetes) who lived around Stockholm Arlanda airport, Eriksson et al found that exposure to higher levels of daily aircraft noise (≥ 50 vs. < 50 dB(A)) was associated with a 19% (95% CI, 3-37%) increase in the incidence of hypertension after adjusting for age and BMI. For those exposed to higher maximum aircraft noise levels (≥ 70 vs. <70 dB(A)), the incidence increased 20% (95% CI, 3-40%). The study found that the elderly and nonsmokers were particularly susceptible to aircraft noise.[20]

A 6-year cohort study with 4860 male participants aged 45-59 years in Berlin found that those exposed to higher levels of road traffic noise ($L_{eq,6\text{-}22h}$, 66-70 vs. 51-55 dB(A)) had a RR of 1.3 (95% CI, 0.8-2.2) for CHD; for those who lived at their residences for at least 15 years at the time of recruitment, the RR was 1.6 (95% CI, 0.9-3.0).[90, 91] In a 5-year Swiss National Cohort Study with 4.6 million subjects, Huss et al found that people exposed to higher levels of aircraft noise (≥ 60 vs. < 45 dB(A)) had a 30% (95% CI, -4 to 76%) increase in MI mortality after adjusting for PM_{10}, residential proximity to major roads, and other covariates; when the analysis was restricted to those who lived in their residences for at least 15 years, the MI mortality increased by 48% (95% CI, 1-118%).[23]

Some evidence has indicated that exposure to occupational noise is associated with an increased risk of cardiovascular disease. In a large retrospective cohort study with 8668 blue-collar sawmill workers in 14 lumber mills in British Columbia, Canada, Davies et al found that the sawmill workers without hearing protection had an 10% (95% CI, 0-20%) increase in acute MI mortality compared with the general population in the province.[92] A

subgroup analysis of this cohort found that exposure to occupational noise levels > 85 dB(A) and >29 years was associated with significantly increased hypertension hospitalization and mortality.[93] A 13-year cohort study with 1804 Finnish male workers aged 40-55 years found that exposure to occupational noise (range, 80-100 dB(A)) was associated with a 1.45-fold (95% CI, 1.04-2.02) increase in CHD hospitalization and mortality after adjusting for age, smoking, BMI, systolic blood pressure, total cholesterol, and shift work.[94]

1.1.7.2 Case-Control Studies

A matched case-control study recruited 1881 patients with MI from 32 major hospitals in Berlin and 2234 controls matched by age, sex, and hospital. Road traffic noise was estimated using a noise map of the city. The study found that for men who lived in the residences with daytime traffic noise levels above 70 dB(A) (vs. ≤ 60 dB(A)) for at least 10 years, the odds ratio of MI was 1.8 (95% CI, 1.0-3.2). An exposure-response relationship was observed in this study. However, the association was not observed among women.[21]

In a population-based case-control study in Stockholm County, Selander et al found that long-term exposure to higher levels of road traffic noise (≥50 vs. <50 dB(A)) was associated with a 12% (95% CI, -5 to 33%) increase in the risk of MI after adjusting for age, sex, smoking status, physical inactivity, diabetes, occupational noise, and NO_2 (indicator of traffic-related air pollution). After further excluding those with hearing loss or with other sources of noise exposure, the risk of MI increased by 38% (95 CI, 1.11-1.71).[22]

In a matched case-control study in England, 1101 male nuclear power workers who died of CHD were matched with surviving controls with similar age and working at the same worksite during the same period. Personal noise exposure was assessed retrospectively by work history records, noise survey records (range, 60-97 dB(A)), and possible use of hearing protection devices. Compared with the unexposed men (the noise immission level, ≤ 85 dB(A)-years), low (85-94.7), medium (94.8-99.6), and high (99.7-110.8) exposure groups had an odds ratio of 1.14 (0.89-1.47), 1.18 (0.90-1.55), and 1.03 (0.76-1.39), respectively, for CHD mortality. Overall, the study did not find a significant association between exposure to occupational noise and coronary mortality.[95]

1.1.7.3 Cross-Sectional Studies

A meta-analysis of cross-sectional studies published between 1970 and 1999 found that when road traffic noise levels increased 5 dB(A), the prevalence of CHD increased 9% (95% CI, -1 to 9%) (range, 51-70 dB(A); 2 original studies), and MI 3% (95% CI, -1 to 9%) (range, 51-80 dB(A); 3 original studies); when aircraft noise levels increased 5 dB(A), the prevalence of hypertension increased 26% (95% CI, 14-39%) (range, 55-77 dB(A); 1 original study); when occupational noise levels increased 5 dB(A), the prevalence of hypertension increased 14% (95% CI, 1-29%) (range, 55-116 dB(A); 9 original studies).[18]

In a cross-sectional study with a large random sample of 38,849 residents in the City of Groningen, the Netherlands, de Kluizenaar et al found that a 10 dB(A) elevation in residential road traffic noise levels (L_{den}) was associated with 31% (95% CI, 25-37%) increase in the prevalence of hypertension (defined as self-reported use of antihypertension

medication). However, after adjusting for age, sex, smoking status, SES, family history of cardiovascular disease, and PM_{10}, the association was substantially decreased and was not statistically significant (OR, 1.03; 95% CI, 0.96-1.11).[96] Another cross-sectional study with a random sample of 667 participants aged 19-80 years in the City of Stockholm found that a 5 dB(A) (range, ≤ 45-65 dB(A)) increase in residential road traffic noise levels was associated with a 38% (95% CI, 6-80%) increase in the prevalence of hypertension after adjusting for age, smoking status, occupational status, and house type. The association was stronger for women (OR, 1.71; 95% CI, 1.17-2.50), those who lived in their residences over 10 years (OR, 1.93; 95% CI, 1.29-2.83), and those who lived in old houses without triple-glazed windows and with bedroom windows facing streets (OR, 2.47; 95% CI, 1.38-4.43).[97]

Recently, in a cross-sectional study with 6307 participants of the US National Health and Nutrition Examination Survey 1999-2004, aged ≥ 20 years, and employed at the time of interview,[98] self-reported exposure (vs. never exposed) to loud occupational noise was associated with a 2-3-fold increase in the prevalence of CHD (OR, 2.04; 95% CI, 1.16-3.58) and isolated diastolic hypertension (OR, 2.23; 95% CI, 1.21-4.12) in an exposure-response fashion. The association of noise exposure with CHD was particularly strong for those participants aged < 50 years, men, and current smokers. There was no significant increase in blood lipids and systemic inflammatory mediators associated with noise exposure.[98]

In summary, there is relatively consistent evidence that noise exposure, including road traffic noise,[18, 19, 21, 22, 90, 91, 96, 97] aircraft noise, [18-20, 23] and occupational noise,[92-95, 98] is

association with increased incidence,[19, 20] hospitalization or mortality,[93] and prevalence[18, 94, 97, 98] of hypertension. But the evidence is not consistent for CHD: there is evidence that noise exposure was associated with increased CHD incidence,[21, 22] mortality, [23, 92, 94] and prevalence;[98] but some studies did not find significant associations of noise exposure with CHD incidence[90, 91] and prevalence[18] (Table 1.3).

1.1.8 Co-Exposure to Air Pollution and Noise on Cardiovascular Disease

In metropolitan areas, road traffic is a major shared source for traffic-related air pollution and community noise. People exposed to traffic-related air pollutants may also be exposed to higher levels of traffic noise and vice versa. For example, Davies et al found that short-term average road traffic noise levels ($L_{eq,5min}$) were moderately correlated with two-week average NO_2 (Pearson correlation r = 0.53) and NO_x (r = 0.64) concentrations measured at 103 roadside sites in metropolitan Vancouver.[61] Ising et al reported that measured residential road traffic noise levels ($L_{eq,\ night}$) were highly correlated with measured daily residential NO_2 concentrations (r = 0.84).[99] Therefore, it is possible that the observed adverse effects of one pollutant such as traffic noise on cardiovascular disease may be confounded or modified by another coexistent pollutant such as traffic-related air pollution and vice versa.

A few recently published epidemiologic studies took into account the influence of coexistent pollutants. In a 9-year Dutch cohort study with 117,528 participants, Beleen et al examined the effects of exposure to both road traffic noise and black smoke on cardiovascular disease mortality. After adjusting for age, sex, smoking status,

neighborhood SES, cardiovascular mortality increased 25% (95% CI, 1-53%) for those exposed to higher levels of road traffic noise (> 65 vs. ≤ 50 dB(A)) and 11% (95% CI, -4 to 28%) in response to a 10 $\mu g/m^3$ increase in black smoke concentrations. In the final model including the above covariates, traffic noise, and black smoke, the corresponding effect estimate was 17% (95% CI, -6 to 45%) for traffic noise and 11% (95% CI, -5 to 28%) for black smoke. These results indicate that the effect estimate for traffic noise was reduced after further adjusting for black smoke (from 25% to 17%); but the effect estimate for black smoke remained almost unchanged after further adjusting for road traffic noise.[89] Like several other studies discussed above that took into account both community noise and air pollution,[23, 96] this study did not examine if exposure to higher levels of both traffic noise and black smoke was associated with greater cardiovascular mortality compared with exposure to higher levels of either single pollutant.[89] However, in a recent case-control study in Stockholm County,[22] Selander et al performed this analysis by dividing study subjects into 3 groups based on road traffic noise levels (<50, 50-57, >57 dB(A)) and NO_2 (indicator of traffic-related air pollution) concentrations (<17, 17-28, >28 $\mu g/m^3$), respectively. Odds ratio (95% CI) for MI was 1.30 (0.76-2.24) for the group exposed to higher levels of noise (>57 dB(A)) but lower levels of NO_2 (<17 $\mu g/m^3$), 1.28 (0.65-2.50) for the group exposed to lower levels of noise (< 50 dB(A)) but higher levels of NO_2 (> 57 $\mu g/m^3$), and 0.95 (0.67-1.33) for the group exposed to both higher levels of noise (> 57 dB(A)) and higher levels of NO_2 (>28 $\mu g/m^3$). These results indicate that there were no positive interactions between road traffic noise and traffic-related air pollution (NO_2) on the risk of MI.[22]

1.1.9 Potential Biological Mechanisms

In addition to convincing epidemiologic evidence for the associations between particulate air pollution and cardiovascular disease, and accumulating epidemiologic evidence for the associations between noise exposure and cardiovascular disease, the understanding of the biological mechanisms for the observed associations has been substantially improved in the recent decade.[11, 12]

1.1.9.1 Air Pollution and Cardiovascular Disease

Ambient air pollutants such as ultrafine carbon particles and soluble components of particulates (e.g. transition metals) can stimulate local inflammatory response in the lung, and activate pulmonary neural reflexes and the autonomic nervous system. They can also readily cross the pulmonary epithelium and enter the systemic circulation to stimulate systemic oxidative stress and inflammatory response. Increased sympathetic activity may contribute to reduced heart rate variability,[100-104]and increased blood pressure[105-107] and heart rate.[100, 108] These direct effects of air pollutants may partly explain acute cardiovascular effects during air pollution episodes.

Ambient air pollutants such as ozone, nitrogen dioxide, and particulates contain reactive oxygen species (ROS) including oxygen ions, free radicals, and peroxides. In addition, airway epithelial cells and macrophages also generate ROS in the process of particle uptake and subsequent redox reactions in cell membrane and mitochondria.[109] ROS are generally small molecules and react indiscriminately with neighboring molecules.[110, 111] When excess ROS come into the lung and the systemic circulation,

cellular antioxidants such as glutathione and vitamin C can be dramatically depleted, resulting in oxidative stress, which can damage cell components including lipids, proteins, and nucleic acids.[110, 111]

Oxidative stress may activate specific transcription factors such as nuclear factor-κB and activator protein-1 to up-regulate gene expression for proinflammatory cytokines (e.g. granulocytemacrophage colony-stimulating factor, tumour necrosis factor-α, and interleukin-1β), chemokines (e.g. interleukin-8, neutrophil activating protein-78), and adhesion molecules (e.g. intercellular adhesion molecule-1).[112, 113] These widespread proinflammatory mediators produced in the lung and the systemic circulation may subsequently activate hemostatic pathways, impair vascular function, and accelerate atherosclerosis.[12, 110]

Controlled exposure studies in humans provide strong pathophysiological evidence in support of a causal relationship between exposure to fine particulate air pollution, particularly black carbon, and adverse cardiovascular effects, although the results are not entirely consistent. Short-term exposure to diesel exhaust or concentrated ambient particles in healthy human volunteers is capable of eliciting acute artery vasoconstriction,[114-116] vascular and endothelial dysfunction,[117, 118] systemic oxidative stress,[118, 119] pulmonary and systemic inflammation,[118, 120-122] enhanced coagulation status, [117-119, 123] elevated blood pressure, [124-126] and decreased heart rate variability.[127-129] As discussed in detail in the 2010 American Heart Association scientific statement,[11] in general, there are three possible pathways linking particulate air pollution and adverse cardiovascular outcomes: (1) oxidative stress and inflammation in the lung and the systemic circulation; (2) imbalance

of autonomic nervous system; and (3) the translocation of ultra fine particles and some components of $PM_{2.5}$ into the systemic circulation. Together, these three pathways may contribute to endothelial cell dysfunction and coronary vasoconstriction; increase blood levels of ROS; promote platelet aggregation and blood coagulation; increase blood pressure and heart rate, and decrease heart rate variability (Figure 1.1).[11, 12]

1.1.9.2 Noise Exposure and Cardiovascular Disease

It is well documented that exposure to community noise such as road traffic noise may cause annoyance, speech interference, sleep disturbance, and psychological stress.[25] Therefore, like general psychosocial stressors that have been demonstrated to be an independent risk factor for cardiovascular disease,[130-132] community noise may serve as a potent human stressor and causes stress response.[133, 134] Noise exposure may arouse the sympathetic nervous system, which may in turn stimulate the endocrine system such as the adrenal gland to release stress hormones including epinephrine (adrenaline), norepinephrine (noadrenaline), and cortisol into the blood stream.[135-137] Stress hormones bind with beta-adrenergic receptors in the heart and blood vessels[138, 139] and cause physiological responses including increased myocardial contractility, arterial pressure, flow velocity,[135-138] and cardiac arrhythmia.[138] Experimental studies in animals have demonstrated that chronic stress and subsequent sympathetic overactivity could induce endothelial injury, platelet accumulation, and coronary atherosclerosis; furthermore, these effects could be prevented by a beta-adrenergic blocking agent.[140] Some experimental studies in humans have showed that chronic stress is associated with systemic

inflammatory cytokine (e.g. tumor necrosis factor-α),[141] endothelial dysfunction,[142] increased blood coagulation and fibrinogen.[132] All these factors may contribute to increased risk of cardiovascular morbidity and mortality (Figure 1.1).

1.1.9.3 Joint Effects of Air Pollution and Noise on Cardiovascular Disease

It is unknown whether there is an interactive effect between air pollution and community noise on cardiovascular disease. However, there is evidence that both air pollutants and noise exposure are capable of activating sympathetic nervous system, leading to increased blood pressure and decreased heart rate variability; both are associated with enhanced blood coagulation, endothelial dysfunction, and systemic inflammation. Theoretically, it is plausible that the coexistence of one pollutant (e.g. community noise) may confound or enhance the effects of another pollutant (e.g. black carbon) on the risk of cardiovascular events (Figure 1.1). However, there has been no epidemiologic or experimental evidence to support this hypothesis.

1.2 Rationale

In urban areas like metropolitan Vancouver, road traffic is a major common source for traffic-related air pollution and community noise.[61, 62] Traffic-related air pollution levels decrease exponentially from major roads and typically approach background levels within about 150 meters.[30, 143] Therefore, the distances between residences and major roads may serve as a simple surrogate for exposure to traffic-related air pollution and road traffic noise.[38, 39] Although several previous studies found that traffic proximity was associated

with the risk of cardiovascular morbidity and mortality,[78, 83, 144, 145] the findings are not entirely consistent.[74, 146] In addition, it is unknown whether changes in traffic proximity could alter the risk. This information is important for evidence-based environmental decision making.

Furthermore, a number of epidemiologic studies have demonstrated that exposure to road traffic is associated with adverse cardiovascular outcomes including coronary artery atherosclerosis,[83] deep vein thrombosis,[147] fatal and non-fatal coronary events,[63, 144, 145] and cardiopulmonary mortality.[77, 78] However, road traffic emissions comprise multiple particulate and gaseous air pollutants,[11, 12, 26] it is uncertain which pollutant(s) are responsible for the adverse cardiovascular outcomes. Identifying these pollutants is important for environmental policy-making and cost-effective air pollution intervention.

Additionally, because of global urbanization, community noise has been increasingly regarded as an important public health problem.[25, 27, 148] In the European Union, all Member States are required to produce noise maps for large urban areas.[87] However, in North America, there is little information about noise exposure in large metropolitan areas. To investigate the associations between exposure to community noise and adverse health effects in large population-based epidemiologic studies, noise exposure assessment for a large number of study subjects is a critical research question.

Finally, the findings from previous studies on the associations between community noise and CHD mortality are not consistent; it is uncertain whether community noise is independently associated with the risk of coronary mortality.[21-23, 89, 90] More importantly, it

is unknown whether community noise may confound or modify the associations between air pollution and coronary mortality and vice versa.

1.3 Objectives

This research aims to investigate the relationships between traffic-related air pollution, community noise, and the risk of CHD morbidity and mortality in metropolitan Vancouver. Specifically, this research includes the following four objectives:

(1) To examine the relationships between residential proximity to road traffic and the risk of CHD mortality including whether living close to major roads is associated with an increased risk and whether changes in traffic proximity could alter the risk.

(2) To examine the relationships between major traffic-related air pollutants and CHD morbidity and mortality, and identify specific traffic-related air pollutants responsible for the observed associations between exposure to road traffic and the risk of CHD events.

(3) To perform community noise exposure assessment using a noise prediction model in the study region and examine the correlations between modeled community noise levels and traffic-related air pollutant concentrations.

(4) To examine the relationships between community noise and CHD mortality as well as the independent and joint effects of community noise and traffic-related air pollution on the risk of CHD mortality.

1.4 Population and Study Design

This research was conducted in metropolitan Vancouver, British Columbia, Canada. The study subjects are a subgroup of the Border Air Quality Study (BAQS) subjects aged 45-85 years who resided in the study region for at least 5 years at baseline (January 1, 1999).[149] The subjects of the BAQS were enumerated using the BC Linked Health Database (BCLHD).[150]

The population-based cohort studies include two periods: a 5-year exposure period (January 1994 - December 1998) and a 4-year follow-up period (January 1999 - December 2002). During the exposure period, residential proximity to road traffic, average concentrations of traffic-related air pollutants including black carbon, $PM_{2.5}$, NO_2, and NO, and annual average community noise levels (in 2003) were estimated at each person's residence. CHD hospitalizations and deaths during the follow-up period were identified from provincial hospitalization databases and death registration databases, respectively.

1.5 Data Sources

1.5.1 British Columbia Linked Health Database

The BCLHD is a large data resource that contains multiple linked administrative databases from provincial health insurance system including provincial health insurance registration records, hospital separation records, outpatient medical service records, vital statistics records, and other health data sources. All these data sources can be linked at individual levels using anonymous individual-specific study identifiers.[150]

The Medical Services Plan (MSP) of British Columbia governed by the Ministry of

Health Services, Government of British Columbia, provides universal health care insurance for the residents in the province. Because enrolment in the health insurance plan is mandatory, almost all residents (over 95%) in the province have registered with the plan except for a minority of the residents including federal employees and some First Nations people covered by Canadian federal health insurance.[151] MSP health insurance registration data provide sociodemographic information including date of birth, sex, and 6-digit residential postal code as well as MSP premium registration information such as start date, and days registered in each fiscal year.

Hospitalization data includes all admission/discharge records from hospitals in British Columbia. This data source provides residential postal code, hospital code, admission date, length of stay, separation date, discharge status (e.g. alive or dead), up to 16 diagnoses (ICD-9 before 2001) or 25 diagnoses (ICD-10 since 2001) to describe the reasons of a hospital admission, and types of diagnosis to explain the role of each diagnosis for a hospital admission and the length of stay. A principal diagnosis is given to the condition most responsible for a hospital admission and the length of stay.

Outpatient medical service data include medical service records provided by general practitioners, specialists, and some supplementary health care practitioners for outpatients registered with the MSP plan. This data source provides residential postal code, service date, practitioner identifier, specialty code, service code, and one diagnosis code (ICD-9) for each medical service.

The death registry from the British Columbia Vital Statistics Agency includes all records of deaths in the province. This data source provides the date of death, sex,

residential postal code, and the cause of death (ICD-10).

Because of privacy restrictions, the complete residential address for study subjects was not provided; as a result, 6-digit residential postal codes were used for exposure assessment. For air pollutants, the pollution levels at the center of a postal code area (area centroid) are assigned to all subjects living in this postal code area. For community noise, the average noise level for an entire postal code area is assigned to all subjects living in this postal code area. In metropolitan Vancouver, a 6-digit postal code typically represents a high-rise building or one side of a city block in urban areas, but may represent a larger area in less densely populated rural areas. Because metropolitan Vancouver is a highly urbanized region, the vast majority of the postal codes represent a small geographic area.

1.5.2 Residential History Construction

A longitudinal residential history during the exposure period and the follow-up period was constructed for each subject using the residential postal codes and associated dates recorded in the BCLHD. About 10% of these records contained invalid postal codes or nonresidential postal codes (e.g. post office boxes) and were excluded. A median of 114 (IQR, 68-181) records were used to construct a person's residential history. When a person changed his/her residences, as indicated by changes in residential postal codes, transition was set as the midpoint between two dates if there was no overlap in two dates**,** or on the first day of the new postal code if there was overlap.

Self-reported residential postal codes were available for a subgroup of the study subjects (n = 1328) who participated in the Canadian Community Health Survey (CCHS)

(cycle 1.1, 2000-2001). A comparison analysis based on the first three digits (Forward Sortation Area) of 6-digit postal codes showed that about 91% of these study subjects had Forward Sortation Areas that were consistent with those reported in the 2001 Survey.

1.6 Exposure Assessment

1.6.1 Residential Proximity to Road Traffic

According to the DMTI ArcView street file dataset (version 2006.3) for British Columbia (DMTI Spatial, Markham, Ontario, Canada) and actual traffic investigation,[152] road types include:

(1) Highway (DMTI type 1 and 2 road): expressway (mean, 114,000 vehicles/day) or principal highway (mean, 21,000 vehicles/day);

(2) Major road (DMTI type 3 and 4 road): secondary highway (mean, 18,000 vehicles/day) or major road (mean, 15,000 vehicles/day).

Traffic volume for each road type in the brackets is average daily traffic counts from actual traffic investigation in this study region.[152]

Based on the previous findings that the concentrations of traffic-related air pollutants typically decrease exponentially from major roads and begin to approach background concentrations within about 150 m, we choose 150 m from a highway or a major road as a surrogate for exposure to traffic-related air pollution.[30, 143, 153] We choose 50 m from a highway or a major road to represent high exposure to traffic-related air pollution.

Distance from each person's residence indicated by the residential postal code (area centroid) to a highway or a major road was measured using GIS software (ArcGIS 9.2, ESRI, Redlands, CA, USA). The buffers of 50 m and 150 m from a highway or a major road were created, respectively. Subjects living within a specific buffer distance were assigned to the exposed group, those who did not were assigned to the unexposed group.

1.6.2 Traffic-Related Air Pollution Exposure Assessment

Land use regression (LUR) models were used to estimate exposures to traffic-related air pollution. The detailed LUR method and data collection process have been described elsewhere.[40, 154, 155] Briefly, to better characterize spatial variability of traffic-related air pollution levels in the study region, LUR models were developed in 2003. During the model building, NO and NO_2 concentrations were measured at 116 sites during two 14-day sampling campaigns, $PM_{2.5}$ concentrations were measured at a subset of 25 sites. Short-term concentrations of particle light absorbance (surrogate for black carbon) were measured in a mobile monitoring campaign on one occasion at a subset of 39 sites.[155] In this study region, the concentrations of black carbon based on particle light absorption coefficient are strongly correlated (R^2 = 0.7-0.8) with traditional measurements of elemental carbon.[156-158]

Based on these measurements and adjustment for temporal variation, annual average concentrations of these air pollutants were calculated for each site. Meanwhile, a total of 55 variables were generated in a GIS (ArcGIS; ESRI, Redlands, CA, USA) to describe the land use characteristics of each site. Measured air pollutant concentrations and

these predictive variables were modeled using multiple linear regression techniques, the most predictive variables were retained in the final model. The coefficient of determination (R^2) for the final model was 0.62 for NO, 0.56 for NO_2, 0.52 for $PM_{2.5}$, and 0.56 for black carbon.

Based on these LUR models, smooth spatial surfaces of predicted annual average concentrations for these air pollutants were generated with a resolution of 10 m. We then applied month-year adjustment factors to each surface to calculate monthly concentrations. The monthly air pollution data were assigned to study subjects through their residential postal codes (area centroids). After integrating changes in residences during the 5-year exposure period, average concentrations of NO, NO_2, $PM_{2.5}$ and black carbon were calculated for each subject.

Chapter 4 describes in detail the model-based community noise exposure assessment in metropolitan Vancouver.

1.7 Coronary Heart Disease Case Definitions

The outcomes of this research include CHD hospitalizations and CHD deaths during the 4-year follow-up period.

(1) CHD hospitalization case: a record of hospitalization with CHD (ICD-9, 410-414 and 429.2; ICD-10, I20-I25) as the principal diagnosis (the most responsible diagnosis) for a hospital admission in the provincial hospitalization database.

(2) CHD death case: a death record with CHD as the cause of death in the provincial death registration database.

(3) Prior CHD cases: subjects who have a hospitalization record with CHD as the principal or primary (the diagnosis that had a substantial influence on hospital length of stay) diagnosis before baseline (based on data from January 1991 to December 1998) are regarded as previously diagnosed CHD cases. These prior CHD cases are excluded from the data analysis.

1.8 Preexisting Comorbidity

Diabetes (ICD-9, 250; ICD-10, E10-E14),[159] chronic obstructive pulmonary disease (COPD) (ICD-9, 490-492 and 496; ICD-10, J40-J44),[160] and hypertensive heart disease (ICD-9, 401-404; ICD-10, I10-I14)[159] are independent risk factors for CHD. Furthermore, these chronic diseases and CHD share common behavioral risk factors such as cigarette smoking. In an effort to control the influence of these preexisting comorbidities and the common behavioral risk factors, all diagnoses in a hospitalization record are used to identify subjects with these comorbidities. One hospitalization record with the diagnosis of any of these diseases during January 1991 to December 1998 is defined as the presence of preexisting comorbidity.

1.9 Neighborhood Socioeconomic Status

The neighborhood-income quintile variable from the 2001 Statistics Canada Census is used to approximate individual SES. For the 2001 Census, the dissemination area is the smallest census geographic unit (400-700 persons) for which all census data are disseminated. Within a census metropolitan area, all dissemination areas are ranked by

household-size adjusted average family income and divided into approximate quintiles, with 1 representing the lowest and 5 representing the highest income quintile. The neighborhood-income quintiles are assigned to study subjects through their residential postal codes.

1.10 Ethical Issues

Behavioral Research Ethics Board at the University of British Columbia approved the study on March 26, 2008 (UBC BREB NUMBER: H08-00185).

Data Access Request Application for BCLHD has been approved by BC Ministry of Health Services.

1.11 List of Chapters

This dissertation comprises six chapters: an introduction chapter, four original research chapters, and a conclusion chapter.

Chapter 1: Introduction.

This chapter includes a literature review of epidemiologic studies on the relationships between air pollution, community noise, and cardiovascular disease; the research objectives; population and study design; and a summary of available data sources.

Chapter 2: Changes in residential proximity to road traffic and the risk of coronary heart disease mortality.

Residential proximity to road traffic was used as a surrogate for exposure to traffic-related air pollution and community noise. This analysis examined whether living close to

major roads was associated with the risk of coronary mortality and whether changes in traffic proximity could alter the risk.

Chapter 3: Long-term exposure to traffic-related air pollution and the risk of coronary heart disease hospitalization and mortality.

Land use regression models were used to estimate residential exposures to major traffic-related air pollutants. The associations of major traffic-related air pollutants with CHD hospitalization and mortality were examine to identify air pollutants responsible for adverse cardiovascular outcomes.

Chapter 4: Modeling population exposure to community noise and air pollution in a large metropolitan area.

A noise prediction model was used to estimate residential exposures to community noise in the study region; this model was evaluated by short-term noise exposure sampling. The correlations between modeled community noise levels and modeled traffic-related air pollution levels were examined; environmental factors that might affect the correlations were discussed.

Chapter 5: Associations of long-term exposure to community noise and traffic-related air pollution with coronary heart disease mortality

The relationships between community noise, traffic-related air pollution, and CHD mortality were examined, with a focus on the independent and joint effects of community noise and black carbon on the risk of CHD mortality.

Chapter 6: Conclusions

The major findings from chapters 2-5 are summarized; the strengths and limitations of this research are discussed; new findings and corresponding policy implications are suggested; and future research to address these limitations is recommended.

Table 1.1 Traditional Risk Factors for Cardiovascular Disease

Tobacco smoke	Advancing age
High blood pressure	Male sex
High blood lipids	Family history
Obesity and overweight	Ethnicity (e.g. Blacks)
Physical inactivity	Menopause for female
Unhealthy diets	
Diabetes mellitus	
Low socioeconomic status	
Psychosocial stress	
Mental ill-health (e.g. depression)	
Alcohol abuse	
Some medications (e.g. oral contraceptives)	
Elevated blood coagulation (e.g. fibrinogen)	
Elevated blood inflammatory markers (e.g. elevated C-reactive protein)	
Excess blood homocysteine	

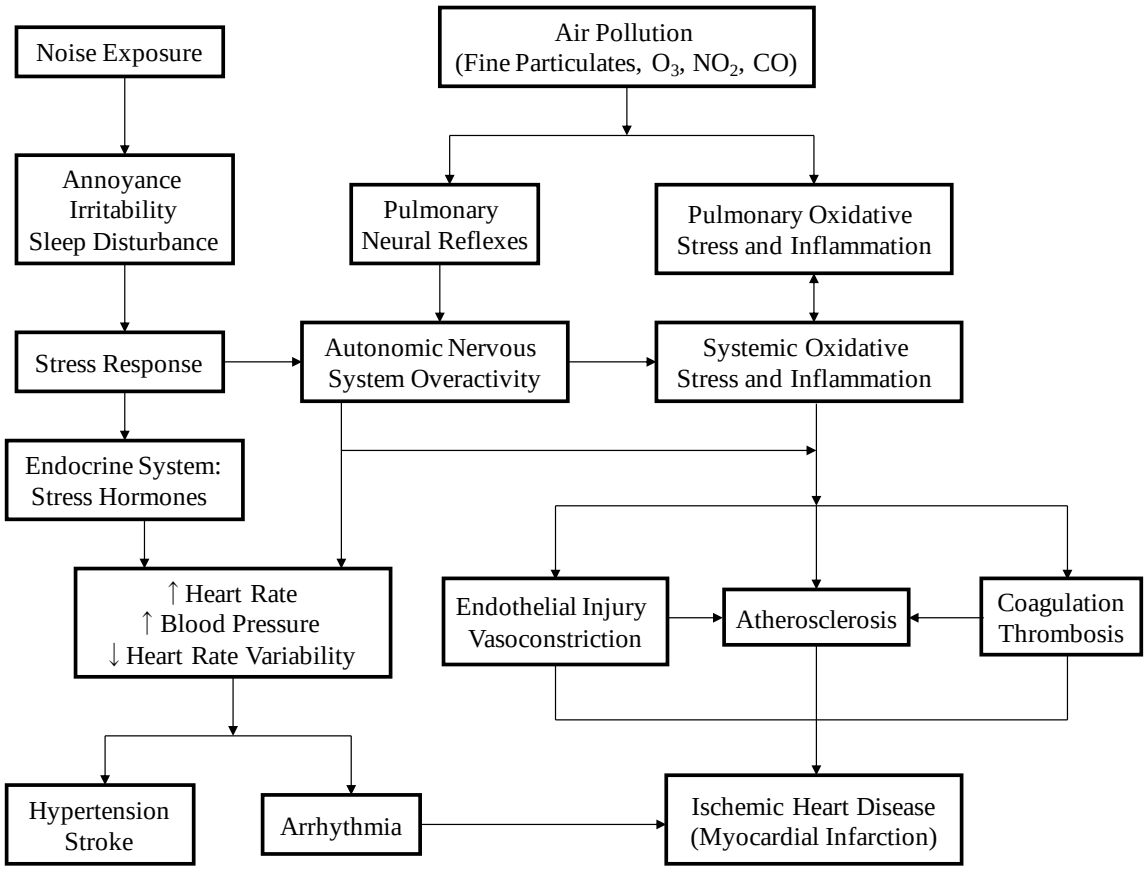
Table 1.2 Cohort Studies of Long-Term Exposure to Air Pollution and Cardiovascular Disease

Source	Region	Sample Size	Age at Baseline	Follow-up Period (year)	Pollutants (μg/m^3)	Comparison	RR (95% CI)	Adjusted Factors
Dockery et al.1993[67]	Six cities in USA	8,111	Mean 50 (25-74)	14-16 (1979-1985)	Citywide exposure mean $PM_{2.5}$: range 11.0-29.6; PM_{10}: range 18.2-46.5	Most vs. least polluted city	Cardiopulmonary mortality: 1.37 (1.11-1.68); All-cause mortality: 1.26 (1.08-1.47)	Age, sex, BMI, and smoking status
Laden et al.2006[68]	Six cities in USA	8,096	Mean 50 (25-74)	24 (1974-1998)	Citywide exposure mean Period 1, 1974-1989, $PM_{2.5}$: range 11.4-29.0; Period 2, 1990-1998, $PM_{2.5}$: range 10.2-22.0	10 μg/m^3 ↑ in $PM_{2.5}$; 10 μg/m^3 ↓ in $PM_{2.5}$	Entire period, Cardiovascular mortality: 1.28 (1.13-1.44); All-cause mortality: 1.16 (1.07-1.26). Decrease in $PM_{2.5}$ from period 1 to 2, Cardiovascular mortality: 0.69 (0.46-1.01); All-cause mortality: 0.73 (0.57-0.95)	Age, sex, BMI, smoking status, pack-years, and education
Pope et al. 2002,[16] 2004[70]	50 States in USA	500,000	≥ 30	16 (1982-1998)	Citywide exposure mean $PM_{2.5}$: mean 17.7, SD 3.7	10 μg/m^3 ↑ in $PM_{2.5}$	CHD: 1.18 (1.14-1.23); Dysrhythmias, heart failure, cardiac arrest: 1.13 (1.05-1.21); Cardiopulmonary mortality: 1.09 (1.03-1.16); All-cause mortality: 1.06 (1.02-1.11)	Age, sex, race, BMI, smoking status, education, marital status, alcohol use, diet, and occupation
Nafstad et al. 2004[79]	Oslo, Norway	16,209	40-49	5 (1974-1998)	Residential exposure mean NO_x: median 10.7, range 0.7-168.3	10 μg/m^3 ↑ in NO_x	CHD mortality: 1.08 (1.03-1.12); Stroke mortality: 1.04 (0.94-1.15)	Age, smoking, education, occupation, physical activity, CVD
Jerrett et al.2005[72]	Los Angeles	22,905	≥ 30	18 (1982-2000)	Zip code area level exposure $PM_{2.5}$: range 9.0-27.1	10 μg/m^3 ↑ in $PM_{2.5}$	CHD: 1.39 (1.12-1.73); Cardiopulmonary mortality: 1.12 (0.97-1.30); All-cause mortality: 1.17 (1.05-1.30)	Age, sex, race, BMI, smoking, education, marital status, alcohol use, diet, etc
Gehring et al.2006[78]	North Rhine-Westphalia, Germany	4,800	50-59	12.9 (1980s-1990s)	Living within a 50-m radius of a major road; Residential exposure: NO_2: mean 39, IQR 29-45; PM_{10}: mean 43.7, IQR 39.8-46.9	IQR ↑ in NO_2, PM_{10}	Cardiopulmonary mortality, Close to a major road: 1.70 (1.02-2.81); NO_2: 1.57 (1.23-2.00); PM_{10}: 1.34 (1.06-1.71); All-cause mortality, NO_2: 1.17 (1.02-1.34); PM_{10}: 1.08 (0.94-1.25)	Smoking status and SES
Miller et al.2007[14]	36 US metropolitan areas	65,893	Median 63 (50-79)	6 (1994-1998)	Residential exposure $PM_{2.5}$: mean 13.5, SD 3.7, range 3.4 to 28.3	10 μg/m^3 ↑ in $PM_{2.5}$	Cardiovascular events: 1.24 (1.09-1.41); Cardiovascular mortality:1.76 (1.25-2.47); Coronary heart disease: 1.21 (1.04-1.42); Cerebrovascular events: 1.35 (1.08-1.68); Stroke: 1.28 (1.02-1.61)	Age, race, BMI, smoking, education, income, systolic blood pressure, comorbidities, etc
Beelen et al.2008[74]	204 municipalities in the Netherlands	120,852	Mean 63 (58-67)	9 (1987-1996)	Residential exposure black smoke: range 9.6-35.8	10 μg/m^3 ↑ in black smoke	Cardiovascular mortality: 1.04 (0.95-1.13) Natural-cause mortality: 1.05 (1.00-1.11)	Age, sex, cigarette smoking, and area-level SES
Rosenlund et al. 2008[36]	Rome, Italy	Residents of Rome	35–84	3 (1998-2000)	Residential exposure NO_2: range 24-73	10 μg/m^3 ↑ in NO_2	Total coronary events: 1.03 (1.00–1.07); Coronary fatal events: 1.07 (1.02–1.12)	Age, sex, and SES

Table 1.3 Cohort and Case-Control Studies of Long-Term Noise Exposure and Cardiovascular Disease

Source	Region	Study Design	Sample Size	Age	Follow-up Period (year)	Noise Level (dB(A))	RR / OR (95% CI)	Adjusted Factors
Babisch et al. 1999 [90, 91]	Berlin, Germany	Cohort study	4,860	45-59 at baseline	6	Road traffic noise: $L_{eq,6\text{-}22\,h}$, 51-70	66-70 vs. 51-55 dB(A) CHD incidence: 1.3 (0.8-2.2)	NA
Babisch et al. 2005[21]	32 hospitals in Berlin, Germany	Matched case-control study	1,881cases, 2,234 controls	57	--	Road traffic noise: $L_{eq,6\text{-}22\,h}$, >70 vs. ≤ 60	MI incidence, All subjects: 1.3 (0.9-1.8); Homes >10 years: 1.8 (1.0-3.2)	Age, BMI, smoking status, work status, education, diabetes, and hypertension
Davies et al. 2005[92]	14 lumber mills in BC, Canada	Retrospective cohort study (occupational noise)	27,464 sawmill workers	Mean 30 (21-36) at baseline	Mean 24, IQR 17-32 (1950-1995)	Threshold at workplace: 85, 90, or 95	8668 workers without hearing protection vs. general population MI mortality: 1.10 (1.1-1.2); CHD mortality: 1.10 (1.1-1.2)	Age, calendar year
McNamee et al. 2006[95]	Nuclear power company in England	Matched case-control study (occupational noise)	1,101 case-control pairs	37 at start of employment	--	Cumulative exposure level (dB(A)-year): unexposed, ≤ 85; low, 85-94.7; medium, 94.8-99.6; high, 99.7-110.8	CHD mortality: Low, 1.14 (0.89-1.47); Medium, 1.18 (0.90-1.55); High, 1.03 (0.76-1.39)	Height, BMI, systolic and diastolic blood pressure, smoking status, and duration of employment
Virkkunen et al. 2006[94]	Five industrial companies in Finland	Cohort study (occupational noise)	1,804	40-55 at baseline	13	80-100 vs. nexposed	CHD hospitalization or mortality: 1.45 (1.04-2.02)	Age, BMI, smoking, systolic blood pressure, total cholesterol, shift work
Eriksson et al. 2007[20]	Around Stockholm Arlanda airport, Sweden	Cohort study	2,027 (half had a family history of diabetes)	35-56 at baseline	10 (1992/1994 to 2002/2004)	Daily average aircraft noise levels: range 60-65; Max. noise levels: range 70-85	Hypertension incidence, Daily averaged noise levels: ≥ 50 vs. < 50 dB(A), 1.19 (1.03-1.37); Max. noise levels: ≥70 vs. <70 dB(A), 1.20 (1.03-1.40)	Age and BMI
Jarup et al.2008[19]	Around six major European airports	Retrospective cohort study	4,861	45-70 at baseline	5	Aircraft noise: L_{night}, 23 pm-7 am, L_{day}, 7 am-23 pm	Hypertension incidence, L_{night}↑10 dB(A): 1.14 (1.01-1.29); L_{day}↑10 dB(A): 1.10 (1.00-1.20)	Age, sex, country, BMI, alcohol intake, education, and physical exercise
Selander et al.2009[22]	Stockholm County	case-control study	1,571 cases, 2,095 controls	45-70	--	Road traffic noise: $L_{Aeq,24h}$ ≥50 vs. <50	Incidence MI, All subjects: 1.12 (0.95-1.33); Subgroup: 1.38 (1.11-1.71)	age, sex, area, smoking status, physical inactivity, diabetes, occupational noise, and NO_2
Huss et al.2010[23]	Swiss National Cohort	Cohort study	4.6 million	>30	5	Aircraft noise: L_{dn} (dB(A)) ≥60 vs. < 45	MI mortality, All subjects: 1.3 (0.96-1.7); Homes ≥ 15 years: 1.5 (1.0-2.2)	Age, sex, marital status, nationality, education, language region, building type, SES, traffic proximity, PM_{10}

Figure 1.1 Potential Biological Mechanisms for the Joint Effects of Air Pollution and Community Noise on Cardiovascular Disease



Chapter 2: Changes in Residential Proximity to Road Traffic and the Risk of Coronary Heart Disease Mortality

2.1 Introduction

A growing body of epidemiologic evidence has demonstrated that long-term exposure to ambient air pollution, especially fine particles, is associated with increased cardiovascular morbidity and mortality.[12, 53] Several cohort studies suggest that coronary heart disease (CHD) is more strongly associated with fine particulate air pollution than are other cardiovascular outcomes.[14, 70] In metropolitan areas, road traffic is a major contributor to air pollution.[30, 43] A European study estimated that approximately half of the adult mortality from air pollution was attributed to traffic-related air pollution.[161] Because exposure to traffic-related air pollution is extensive worldwide, the corresponding adverse cardiovascular effects may represent an important public health problem.[12]

The concentrations of traffic-related air pollutants decrease exponentially from major roadways and typically approach background concentrations within about 150 meters.[30, 143] The distances from residences to major roadways may therefore reflect spatial variability in the concentrations of traffic-related air pollutants. Although traffic proximity may also be associated with other exposures such as traffic noise, it can serve as a simple and policy-relevant surrogate for exposure to traffic-related air pollution.[38, 39] This metric has been widely used in epidemiologic studies of the health effects of traffic-related air pollution.[35, 36, 38, 39, 74, 78, 79, 83, 144-146]

There have been a number of epidemiologic studies examining the associations between residential proximity to road traffic and adverse cardiovascular outcomes including arterial atherosclerosis[83, 146] and CHD morbidity and mortality.[35, 36, 74, 78, 79, 144, 145] Although most of these

studies have reported significant associations, the findings are not entirely consistent. One critical limitation of these studies is the assumption that baseline residential exposure status is consistent during the entire follow-up period; residential relocation after baseline enrollment has generally been ignored. This unrealistic assumption may result in exposure misclassification, and thus bias effect estimates toward the null.

We conducted a large population-based cohort study with detailed residential history information to investigate the association between residential proximity to road traffic and the risk of CHD mortality. Specifically, we examined the following factors: (1) whether residential proximity to traffic was associated with higher levels of exposure to traffic-related air pollution; (2) whether living close to traffic was associated with an increased risk of CHD mortality; and (3) whether changing residences, and therefore changing proximity to traffic, was associated with an altered risk of CHD mortality.

2.2 Methods

2.2.1 Study Design

This population-based cohort study was conducted in metropolitan Vancouver, Canada. We used linked administrative databases from British Columbia's universal health insurance system to assemble a population-based cohort. This study included two stages: a 5-year exposure period (January 1994 - December 1998) and a 4-year follow-up period (January 1999 - December 2002). Mortality information during the follow-up period was identified from provincial vital statistics records. CHD mortality was compared between study subjects with different residential-traffic-exposure profiles to determine the relationship between residential proximity to traffic and the risk of

CHD mortality. This study was approved by the Institutional Review Board of The University of British Columbia (Behavioural Research Ethics Board certificate # H08-00185).

2.2.2 Study Cohort

All metropolitan Vancouver residents who met the following criteria at baseline (January 1999) were included in the cohort: (1) registered with the provincial health insurance plan, which provides universal coverage to the resident population; (2) age 45 to 85 years; and (3) without previous diagnosis of CHD. A small number (4%) of study subjects who moved to other regions of the province during the 5-year exposure period were included, all other subjects remained in the study region during the exposure period.

2.2.3 Residential Proximity to Road Traffic

Depending on road types (highway or major road) and distance (50 m or 150 m) from major roadways, residential proximity to road traffic included 5 exposure categories: (1) ≤ 50 m versus > 50 m from a highway; (2) ≤ 150 m versus > 150 m from a highway; (3) ≤ 50 m versus > 50 m from a major road; (4) ≤ 150 m versus > 150 m from a major road; (5) ≤ 150 m from a highway or ≤ 50 m from a major road versus > 150 m from a highway or > 50 m from a major road.

Based on individual residential histories and if residential postal codes (area centroids) were located within 50 m or 150 m of major roads during the exposure period and the follow-up period, for each traffic exposure category, the study subjects were divided into 4 groups:

1. Not exposed to traffic: consistently living away from traffic;
2. Consistent exposure to traffic: consistently living close to traffic;

3. Moved close to traffic: changing residence from non-exposed to exposed to traffic during the exposure period and retaining this exposure status until the end of follow-up;
4. Moved away from traffic: changing residence from exposed to non-exposed to traffic during the exposure period and retaining this non-exposure status until the end of follow-up.

Subjects with more than one change in exposure status (e.g. those who changed residences from non-exposed to exposed and then changed back to non-exposed or vice versa) during the exposure period were excluded from the study; those who changed their exposure status during the follow-up period were also excluded from the study.

2.2.4 Traffic-Related Air Pollution Exposure Assessment

We used high resolution land use regression (LUR) models to estimate exposure levels to traffic-related air pollutants including black carbon, $PM_{2.5}$, nitrogen dioxide (NO_2) and nitric oxide (NO). Since the air pollution measurements did not cover the whole study region, air pollution data were only available for a subgroup of the cohort.

Using detailed residential history and corresponding monthly concentrations of traffic-related air pollutants during the 5-year exposure period, average concentrations of air pollutants were calculated for each subject. The detailed methods for the measurement of air pollutants in this study have been described elsewhere.[40, 154]

2.2.5 Coronary Heart Disease Mortality

A case of CHD death was defined as a death record in the provincial death registration database with CHD (ICD-9 codes 410-414, 429.2 and ICD-10 codes I20-I25) as the cause of death.

A small proportion of deaths were identified using provincial hospitalization records: a hospitalization death record with CHD as the principal diagnosis for a hospital admission.

Subjects who had a hospitalization record with CHD as the principal or primary diagnosis before baseline (based on available data from January 1991 to December 1998) were regarded as previously diagnosed CHD cases and were excluded from the analysis.

2.2.6 Preexisting Comorbidity

Chronic obstructive pulmonary disease (COPD)[160] (ICD-9: 490, 491, 492, 496; ICD-10: J40-J44), diabetes[159] (ICD-9, 250; ICD-10, E10-E14), and hypertensive heart disease[159] (ICD-9: 401-404; ICD-10: I10-I14) are independent risk factors for CHD. In addition, these chronic diseases and CHD share common behavioral risk factors such as cigarette smoking. In an effort to control the influence of the comorbidities and these common behavioral risk factors, all diagnoses (not restricted to principal diagnosis) in a hospitalization record were used to identify subjects with these comorbidities. One hospitalization record with the diagnosis of any of these diseases during January 1991 to December 1998 was defined as the presence of preexisting comorbidity.

2.2.7 Neighborhood Socioeconomic Status

Individual-level income data were not available in this study. We used neighborhood-income quintiles from the 2001 Statistics Canada Census data to approximate a subject's socioeconomic status (SES). Neighborhood-income quintiles were assigned to study subjects through their residential postal codes.

2.2.8 Statistical Analysis

We compared the baseline characteristics among the exposure groups using a chi-square test for categorical variables, one-way analysis of variance (ANOVA) for continuous variables, and Tukey's post hoc analysis for pair-wise comparisons of continuous variables. Similarly, in a subgroup analysis for the subjects with air pollution data, we used ANOVA and Tukey's post hoc analysis to determine whether residential traffic exposure profiles were associated with exposure levels to traffic-related air pollutants.

To determine the association between residential proximity to road traffic (predictor variable) and the risk of CHD mortality (dependent variable), we first performed bivariable logistic regression analysis using the non-exposed group as the reference category. Then we performed multivariate logistic regression analysis to adjust for age, sex, neighborhood income quintiles, and comorbidity including diabetes, COPD, or hypertensive heart disease (yes or no). These analyses were repeated for different combinations of road types (highway or major road) and distances (50 m or 150 m).

To examine the influence of age and sex on the risk of CHD mortality associated with traffic exposure, we performed stratified analyses by age (< 65 years, ≥ 65 years) and sex, using the exposure category 150 m from a highway or 50 m from a major road.

The exposure category " $\leq$50 m versus >50 m from a highway" had the largest effect estimates, we therefore used this category to perform a sensitivity analysis in which we compared the relative risks of CHD mortality using various distances from a highway and various frames of reference.

All analyses were performed using SAS 9.1 (SAS Institute Inc., Cary, NC, USA).

2.3 Results

We use the road traffic exposure category "150 m from a highway or 50 m from a major road" to present the results of this study. At baseline in January 1999, there were 488,785 subjects who met the inclusion criteria. At the end of follow-up, 38,502 persons (7.9%) were lost to follow-up, mainly due to moving out of the province or dying from other diseases. This left 450,283 subjects with complete data; 210,128 persons (46.7%) changed their residences at least one time during the 9-year study period, and 68,726 persons (15.3%) changed their exposure status. We excluded 12,619 persons (2.8%) with multiple changes in exposure status and 22,871 (5.1%) who changed their exposure status during the follow-up period. This left 414,793 subjects for analysis: 328,609 (79.2%) consistently lived away from traffic, 52,948 (12.8%) consistently lived close to traffic, 15,747 (3.8%) moved close to traffic, and 17,489 (4.2%) moved away from traffic (Table 2.1).

The baseline characteristics of these subjects are summarized by the 4 exposure groups in Table 2.1. Fewer than half (46.1%) of the subjects were male; the average age (SD) was 59 (11) years (range, 45-83 years). Overall, compared with those consistently living away from traffic, persons who consistently lived close to traffic were older and more likely to have lower neighborhood SES and preexisting comorbidity (Table 2.1).

Based on the LUR data that incorporated high spatial resolution, persons who consistently lived close to traffic were exposed to elevated concentrations of black carbon, $PM_{2.5}$, NO_2, and NO during the 5-year exposure period (Table 2.2). Furthermore, those once living close to traffic were also exposed to higher concentrations of black carbon, NO_2, and NO; this increment was even larger for those who moved their residences close to traffic (Table 2.2).

During the follow-up period, 3133 people (3097 from the death registration database and 36 from hospitalization records) died of CHD, for an overall mortality rate of 7.6 per 1000 subjects.

Compared with subjects consistently living away from traffic, those consistently living close to traffic were 69% [95% confidence interval (CI), 55-85%] more likely to die of CHD during the follow-up period. For those who moved away from traffic during the exposure period, there was a 4% increase in the risk of CHD mortality (0.87-1.25) during the follow-up period compared with the unexposed. For those moving closer to traffic during the exposure period, the risk of CHD mortality increased 23% (1.03-1.46) as compared with the unexposed. Adjustment for baseline age, sex, preexisting comorbidity, and neighborhood SES generally reduced the relative risks but did not change the overall pattern of the results: the risk of CHD mortality increased by 29% (1.18-1.41), 14% (0.95-1.37), and 20% (1.00-1.43), respectively, for those consistently living close to traffic, moving away from traffic, and moving close to traffic (Table 2.3).

Similar CHD mortality patterns were observed when the above analysis was repeated using different road types and distances (Table 2.3, Figure 2.1). Figure 2.1 shows that the risk of CHD mortality was strongly dependent on road types (traffic volume) and the distances from major roads. For example, for those consistently living close to traffic, the risk of CHD death rapidly decreased when the distance from traffic increased from 50 m to 150 m or when road type changed from a highway (21,000-114,000 vehicles/day) to a major road (15,000-18,000 vehicles/day). Overall, compared with consistently living away from traffic (x axis), consistently living close to traffic was associated with the highest risk of CHD mortality (Figure 2.1); moving close to traffic was associated with an elevated but lower risk compared with consistently living close to traffic; moving away from traffic was associated with a decreased but higher risk compared with consistently living away from traffic.

For those consistently living within 150 m from a highway or 50 m from a major road (versus consistently living >150 m from a highway or >50 m from a major road), the risk of CHD mortality

was higher for men than for women, and higher for the younger (< 65 years) than for the older group (≥ 65 years) (Figure 2.2)

In the sensitivity analysis examining the effects of distances and reference groups, for those who moved away from traffic during the exposure period, the effect estimates were very close amongst the three groups. However, for those who moved close to or consistently lived close to traffic, the effect estimates changed in response to different distances and references used in the analysis (Figure 2.3), indicating that the observed association between residential proximity to traffic and the risk of CHD mortality was sensitive to distances from highways and references used for comparison.

2.4 Discussion

In this large population-based cohort study with detailed residential history information, living close to traffic was associated with an increased risk of CHD mortality. More importantly, a change in residential proximity to traffic was associated with an altered risk of CHD mortality: moving close to traffic was associated with a relatively increased risk, whereas moving away from traffic was associated with a relatively decreased risk.

Previous studies examining the associations between residential proximity to traffic and cardiovascular outcomes have not reported entirely consistent findings. A cross-sectional study with 4494 participants in Germany found that living close to a major road was associated with more severe coronary artery calcification.[83] In contrast, a recent study with 1147 participants in the United States found no appreciable association between residential proximity to a major road and abdominal aortic calcification.[146] In a 13-year cohort study of 13,309 participants in the United States, Kan et al found that residential traffic intensity was associated with an increased risk of fatal and nonfatal

coronary events.[144] Similarly, in a large case-control study, Tonne et al reported that living near a major road was associated with a 5% increase in the risk of acute myocardial infarction.[145] A 13-year cohort study of 4,800 women in Germany also found that living within a 50 m of a major road was associated with increased cardiopulmonary mortality.[78] In contrast, in a 9-year Dutch cohort study with 117,528 participants, Beelen et al did not find an association between residential proximity to a major road or residential traffic intensity and cardiovascular mortality.[74] Several studies have also reported associations between exposures to traffic-related air pollutants such as nitrogen oxides and adverse cardiovascular outcomes.[35, 36, 79] Because of differences in traffic characteristics, study populations, meteorological and geographic conditions, study design, and statistical methods, it is difficult to quantitatively compare the results from different studies. Although the findings from these previous studies are not fully consistent, the present study and most previous studies suggest that residential proximity to traffic is associated with an increased risk of CHD mortality. Traffic-related air pollution and other factors such as traffic noise may be responsible for the observed association.

Compared to previous reports, this study has several important strengths: First, this population-based cohort study may be regarded as a natural experiment in which we took advantage of detailed residential histories to investigate the relationship between changes in traffic exposure status and the risk of CHD mortality. Change in residential proximity to traffic was associated with an altered risk of CHD mortality in an exposure-response fashion.

Second, we used various road types (highway or major road) and distances ($\leq$ 50 m or $\leq$ 150 m) from major roads to assess residential proximity to traffic. The observed association was consistent across various combinations of road types and distances. The effect estimate was

dependent on road types (traffic volume) and distances in a dose-response fashion (Table 2.3, Figure 2.1).

Third, residential proximity to traffic was consistent with land-use-regression-model estimates for the concentrations of black carbon, NO_2, and NO (Table 2.2). These results are consistent with those of previous studies and suggest that residential proximity to traffic is a simple and specific surrogate that is able to reflect spatial variability of traffic-related air pollution.[30, 43] In a separate analysis of associations between these 4 pollutants and the risk of CHD mortality, we found that an interquartile range elevation in the concentrations of black carbon was associated with a 6% (95% CI, 3-9%) increase in the risk of CHD mortality after adjustment for all the covariates and 3 other copollutants ($PM_{2.5}$, NO_2, and NO); the corresponding relative risk for $PM_{2.5}$, NO_2, and NO was 1.00 (0.96-1.03), 1.03 (0.99-1.07), and 1.03 (0.99-1.08), respectively.[162]

Fourth, this study found that 46.7% of study subjects changed their residences at least one time during the 9-year study period, leading to a change in the residential traffic exposure status in 15.3% of the subjects. When residential proximity to traffic at the original address (January 1994) was used to evaluate traffic exposure status (and subsequent residential relocations were ignored), the corresponding adjusted RRs (95% CIs) for each of 5 exposure categories were 1.19 (1.10-1.29), 1.34 (1.10-1.64), 1.27 (1.13-1.42), 1.09 (0.99-1.21), and 1.06 (0.99-1.14) (Table 2.3, from the first to the fifth row). Thus, previous studies that have not accounted for residential relocation may have suffered from substantial exposure misclassification. This may result in underestimations of the true adverse health effects, and even false-negative results.

This study also had several limitations that should be considered when interpreting these findings. The study cohort was constructed using linked administrative databases that did not include certain important information about individual cardiovascular risk factors (such as active or passive

smoking status, body mass index, and individual SES). To partially control for these unmeasured risk factors, we adjusted for age, sex, neighborhood SES, and preexisting comorbidity including diabetes, COPD, and hypertensive heart disease. Because these comorbidities and CHD share common behavioral risk factors, adjusting for these comorbidities was presumably able to reduce the influence of uncontrolled factors, such as cigarette smoking, to some extent.[163] However, these approaches cannot eliminate all confounding effects caused by unmeasured cardiovascular risk factors.

Cigarette smoking is the single most important risk factor for CHD.[164] If smokers are more likely to live or move closer to major roadways, the observed association may be confounded by cigarette smoking. However, previous epidemiologic studies have demonstrated that the association of air pollution exposure with the severity of atherosclerosis[83, 84] or the risk of CHD mortality[16, 70] was independent of cigarette smoking status and even stronger among never-smokers.[16, 70, 83, 84] For example, Pope et al reported that for each 10 $\mu g/m^3$ increase in annual average concentration of $PM_{2.5}$, the adjusted relative risk of CHD mortality was 1.22 for never smokers, 1.15 for former smokers, and 1.16 for current smokers.[70] Given these findings and the lack of evidence to suggest that cigarette smoking is related to changes in residential proximity to traffic, it is less likely that the observed associations were due to confounding effects of cigarette smoking.

Low SES is a risk factor for CHD[165] and also related to other cardiovascular risk factors including cigarette smoking, obesity, and hypertension.[166-168] In some locations, people with low SES are more likely to live close to roadways.[169] Individual SES is thus a possible confounder for the observed association. In the present study, we used neighborhood income quintiles to approximate the major differences of economic status between subjects with various traffic exposure profiles. Although this method may induce a degree of SES misclassification, some evidence has suggested that this approximation is acceptable for group comparisons.[170, 171] In addition, some studies have

found that neighborhood SES was associated with the risk of CHD independent of individual SES, indicating that adjustment for neighborhood SES may also reduce the influence of uncontrolled factors related to neighborhood disadvantages.[168] We used neighborhood income quintiles derived from the 2001 census data, which may not accurately reflect the original neighborhood SES for subjects who changed their residences during the exposure period (January 1994 - December 1998). Nevertheless, there is evidence that the levels of neighborhood SES are well correlated for those who change their residences.[168]

It should be noted that residential proximity to traffic is a relatively crude surrogate for exposure to traffic-related air pollution. Many factors, such as wind direction, presence of street canyons, and specific residence characteristics, may influence the actual residential exposure levels.[172, 173] Moreover, in the present study, residential proximity to traffic was estimated using the postal code centroid rather than the actual residential address. In urban areas, a 6-digit postal code typically represents one side of a city block or individual multi-unit structures and is therefore fairly precise. Still, this assessment of traffic proximity will inevitably induce exposure misclassification. Furthermore, as in previous studies, our exposure assessment can only approximately reflect the exposure levels at subjects' residences, which may not precisely reflect actual individual exposure levels. Mobility[52], outdoor activity, and indoor infiltration of air pollutants[51] may differ across study subjects. Nevertheless, all these factors presumably cause non-differential exposure misclassification, leading to underestimations of the true adverse effects of residential proximity to traffic.

Finally, residential proximity to traffic signifies exposure not only to traffic-related air pollutants but also to traffic-related noise. Some studies have indicated that traffic noise levels are at least moderately correlated with the concentrations of nitrogen oxides[61] and are also associated with an increased risk of CHD.[21] Therefore, it is possible that the increased risk of CHD mortality

observed in the present study may be associated with both traffic-related air pollution and traffic noise. We cannot disentangle the effects of these two traffic-related pollutants in current analysis.

An enormous number of people are regularly exposed to traffic; therefore, traffic-related air pollution may represent an important public health problem. Using a large population-based cohort study with detailed residential history information, we observed that living close to traffic was associated with an increased risk, whereas moving away from traffic was associated with a decreased risk, of coronary mortality.

Table 2.1 Baseline Characteristics of Study Subjects by Exposure Groups

Covariate[a]	Not Exposed to Traffic (n = 328,609)	Moved Close to Traffic (n = 15,747)	Moved Away From Traffic (n = 17,489)	Consistent Exposure to Traffic (n = 52,948)
Men (%)	46.2	46.2	46.8	44.8
Age (SD) (year)	58.7 (10.4)	58.6 (10.2)	57.6 (10.0)	61.0 (10.9)
Age quintiles (%)				
45-48	18.8	18.8	21.3	14.8
49-53	21.6	21.4	22.6	17.6
54-60	20.5	20.7	20.8	19.1
61-69	19.82	21.1	19.9	22.0
70-83	19.3	18.1	15.4	26.4
Comorbidity (%)				
Diabetes	1.9	2.1	2.0	2.5
COPD	1.0	1.2	1.2	1.5
Hypertensive heart disease	3.7	4.0	3.9	4.6
Any of the above	5.6	6.4	6.1	7.2
Income quintiles (%)[b]				
1	14.9	24.9	19.5	26.8
2	18.0	19.3	18.8	19.6
3	19.4	20.9	19.8	18.5
4	21.7	17.7	22.3	16.3
5	26.0	17.3	19.7	18.9

Abbreviations: COPD, chronic obstructive pulmonary disease.

[a] Traffic exposure was defined as ≤ 150 m from a highway or ≤ 50 m from a major road. Overall comparison for each variable is statistically significant.

[b] Quintile 1 represents the lowest and Quintile 5 the highest income quintile.

Table 2.2 Average Concentrations of Traffic-Related Air Pollutants by Exposure Groups

Air Pollutant[a]	Not Exposed to Traffic (n = 306,296)	Moved Close to Traffic (n = 13,285)	Moved Away From Traffic (n = 14,582)	Consistent Exposure to Traffic (n = 50,502)
Black carbon (10^{-5}/m)	1.1 ± 0.7	2.3 ± 1.1	1.9 ± 0.9	3.0 ± 1.5
$PM_{2.5}$ ($\mu g/m^3$)	4.0 ± 1.6	4.2 ± 1.6	4.1 ± 1.6	4.3 ± 1.8
NO_2 ($\mu g/m^3$)	31.3 ± 7.9	33.9 ± 7.5	33.0 ± 7.6	35.5 ± 7.9
NO ($\mu g/m^3$)	28.8 ± 8.2	39.5 ± 13.4	34.8 ± 10.7	45.9 ± 16.6

[a] This is a sub-group analysis for the subjects (93% of cohort) with land use regression data (expressed as mean ± SD). Traffic exposure was defined as ≤ 150 m from a highway or ≤ 50 m from a major road. Overall comparisons and pair-wise comparisons (with non-exposed group) are statistically significant.

Table 2.3 RRs (95% CIs) of Coronary Heart Disease Mortality by Exposure Groups

Exposure Category	Not Exposed to Traffic[a]	Moved Close to Traffic	Moved Away From Traffic	Consistent Exposure to Traffic
150 m Highway or 50 m major road				
No. deaths/total number	2271/328,609	131/15,747	124/17,489	607/52,948
Crude RR (95% CI)	1.00	1.23 (1.03-1.46)	1.04 (0.87-1.25)	1.69 (1.55-1.85)
Adjusted RR (95% CI)[b]	1.00	1.20 (1.00-1.43)	1.14 (0.95-1.37)	1.29 (1.18-1.41)
50 m Highway				
No. deaths/total number	3164/434,602	26/2304	21/2729	73/4343
Crude RR (95% CI)	1.00	1.55 (1.05-2.29)	1.05 (0.69-1.62)	2.33 (1.84-2.94)
Adjusted RR (95% CI)[b]	1.00	1.44 (0.97-2.13)	1.09 (0.71-1.69)	1.54 (1.21-1.96)
150 m Highway				
No. deaths/total number	2851/397,341	59/7016	62/8484	257/20,085
Crude RR (95% CI)	1.00	1.18 (0.91-1.53)	1.02 (0.80-1.32)	1.80 (1.59-2.05)
Adjusted RR (95% CI)[b]	1.00	1.22 (0.94-1.59)	1.11 (0.86-1.44)	1.36 (1.19-1.55)
50 m Major road				
No. deaths/total number	2674/370,505	90/10,534	88/12,935	330/31,073
Crude RR (95% CI)	1.00	1.20 (0.97-1.48)	0.95 (0.77-1.18)	1.49 (1.33-1.67)
Adjusted RR (95% CI)[b]	1.00	1.16 (0.93-1.43)	1.07 (0.86-1.33)	1.15 (1.02-1.29)
150 m Major road				
No. deaths/total number	1752/247,483	157/19,724	170/25,781	1024/112,093
Crude RR (95% CI)	1.00	1.17 (1.00-1.38)	0.97 (0.83-1.14)	1.35 (1.25-1.46)
Adjusted RR (95% CI)[b]	1.00	1.24 (1.05-1.46)	1.09 (0.93-1.28)	1.11 (1.02-1.19)

The total number of subjects in each exposure category is different due to exclusion of subjects who irregularly changed their exposure status and who changed the exposure status during the follow-up period.

[a] Reference category.

[b] Adjusted for age, sex, neighborhood SES, and preexisting comorbidity.

Figure 2.1 Adjusted RRs of Coronary Heart Disease (CHD) Mortality by Road Types and Distances

Adjusted for age, sex, neighborhood SES, and preexisting comorbidity.

[a]Versus > 150 m Highway or > 50 m Major Road.

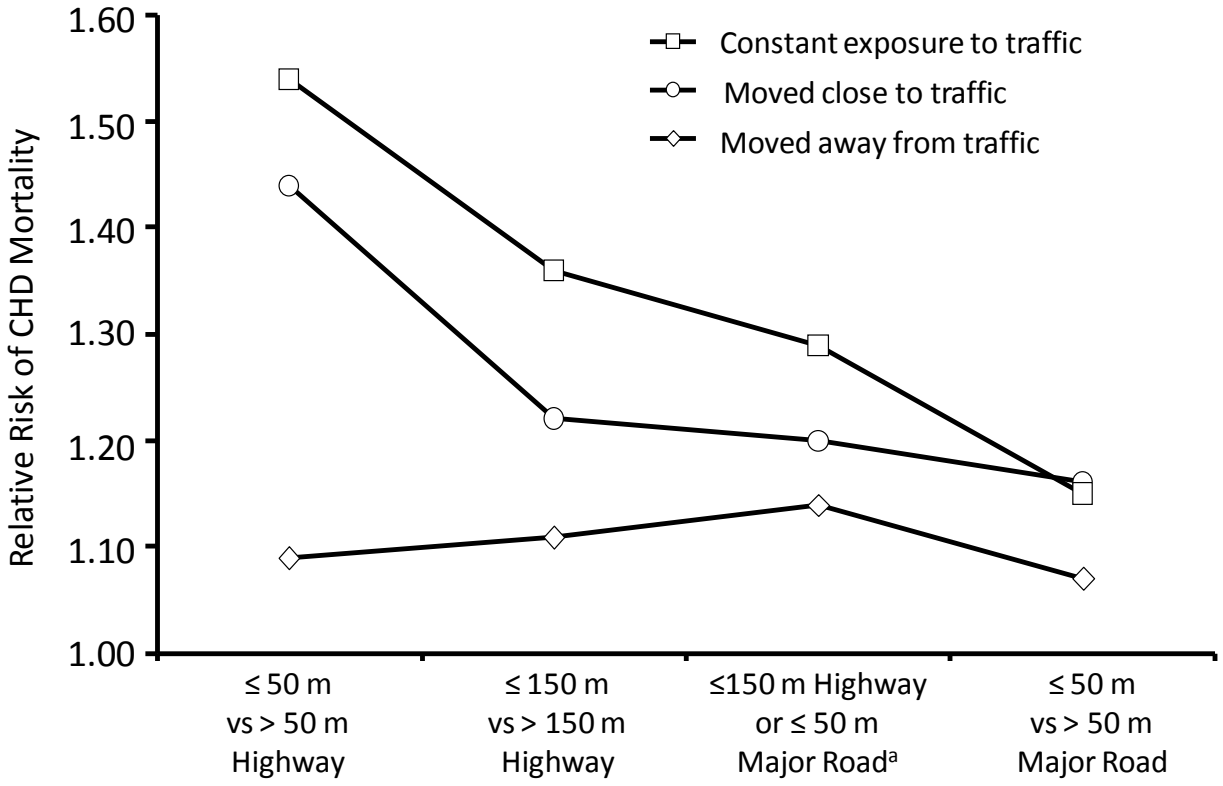


Figure 2.2 Adjusted RRs and 95% CIs of Coronary Heart Disease (CHD) Mortality by Sex and Age

The exposure category, 150 m from highway or 50 m from major road, was used for the analyses.

Adjusted for neighborhood SES and preexisting comorbidity; the combined analyses ("Both") were additionally adjusted for age (< 65 years, ≥ 65 years); for the total group, the analyses were additionally adjusted for age (<65 years, ≥ 65 years) and sex.

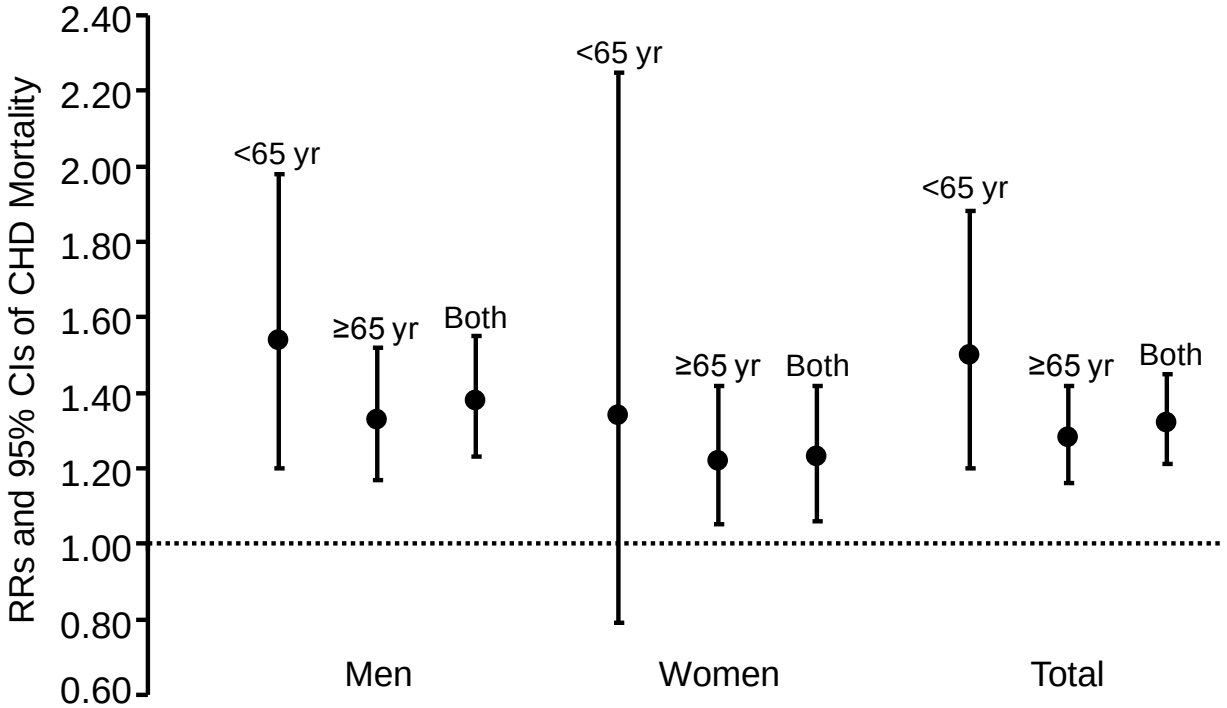
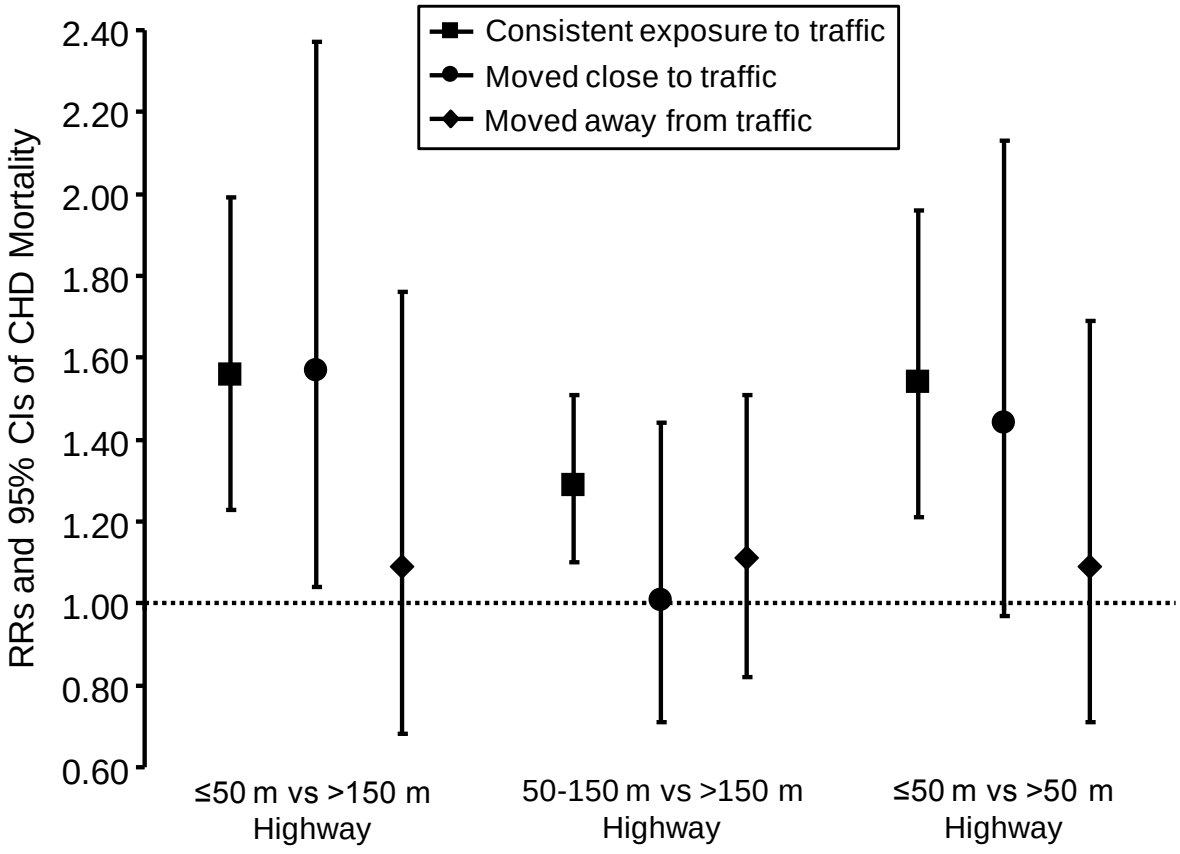


Figure 2.3 Adjusted RRs and 95% CIs of Coronary Heart Disease (CHD) Mortality by Distances from Highways

Adjusted for age, sex, neighborhood SES, and preexisting comorbidity.



Chapter 3: Long-Term Exposure to Traffic-Related Air Pollution and the Risk of Coronary Heart Disease Hospitalization and Mortality

3.1 Introduction

A number of epidemiologic studies have demonstrated that long-term exposure to road traffic as indicated by residential proximity to major roadways or residential traffic intensity is associated with adverse cardiovascular outcomes including coronary artery atherosclerosis,[83] deep vein thrombosis,[147] fatal and non-fatal coronary events,[144, 145] and cardiopulmonary mortality.[77, 78] In a previous analysis of this population-based cohort,[174] we observed that living close to road traffic was associated with an increased risk of coronary heart disease (CHD) mortality and that change in residential proximity to road traffic was associated with an altered risk of CHD mortality: moving close to traffic was associated with an increased risk, whereas moving away from traffic was associated with a decreased risk. In addition to exposure to traffic noise,[22] residential proximity to road traffic may reflect exposure to multiple traffic-related air pollutants.[30, 43, 161] Identifying traffic-related air pollutants responsible for adverse cardiovascular outcomes is important for evidence-based environmental policy making and cost-effective air pollution intervention.

Metropolitan Vancouver, located on the west coast of Canada, has relatively low levels of air pollution compared with other metropolitan areas. For example, in this region, the annual average concentration of fine particles (aerodynamic diameter $\leqslant$2.5 μm; $PM_{2.5}$) is 5 $\mu g/m^3$,[40] in contrast to 8.7 $\mu g/m^3$ in Toronto, Canada,[175] 14.0 $\mu g/m^3$ across metropolitan areas of the United States,[70] 28.3 $\mu g/m^3$ in the Netherlands,[74] and 22.8 $\mu g/m^3$ in the Ruhr area, Germany.[83] As in most urban areas,

motor vehicles are recognized as a major contributor to ambient air pollution and is responsible for much of the spatial variability in pollutant concentrations.[154]

Based on our previous analyses,[174] we conducted a large population-based cohort study to identify specific traffic-related air pollutants that might be responsible for the observed association between exposure to road traffic and the risk of CHD mortality. We also examined the relationships between traffic-related air pollutants and the risk of CHD hospitalization.

3.2 Methods

3.2.1 Study Design

This population-based cohort study included two periods: a 5-year exposure period (January 1994 to December 1998) and a 4-year follow-up period (January 1999 to December 2002) for which mortality data were available. Average concentrations of traffic-related air pollutants were estimated at residences of subjects using land use regression (LUR) models and integrating changes in residences during the exposure period. Hospitalization and mortality information during the follow-up period was retrieved from provincial hospitalization records and death registration records, respectively. This study was approved by the Institutional Review Board of The University of British Columbia (Behavioural Research Ethics Board certificate # H08-00185).

3.2.2 Population

As described previously, we used linked administrative databases from the universal health insurance system of British Columbia to assemble a population-based cohort.[174] All metropolitan Vancouver residents who met the following criteria at baseline (January 1999) were included in the cohort: registered with the provincial health insurance plan, which provides universal coverage to

nearly all residents in the study region; resided in the study region during the 5-year exposure period; 45 to 85 years of age; and no previous diagnosis of CHD.

3.2.3 Air Pollution Exposure Assessment

We used a high-resolution LUR model combined with residential histories to estimate individual exposure to traffic-related air pollutants including black carbon, $PM_{2.5}$, nitrogen dioxide (NO_2) and nitric oxide (NO) during the 5-year exposure period. This method has been described in detail elsewhere.[40, 154, 155] Briefly, NO and NO_2 concentrations were measured using Ogawa passive samplers (Ogawa USA, Pompano Beach, FL, USA) at 116 sites. $PM_{2.5}$ concentrations were measured using Harvard Impactors (Air Diagnostics and Engineering, Harrison, ME, USA) at a subset of 25 locations. Light absorbing carbon (black carbon) concentrations were measured using a particle soot absorption photometer (Radiance Research, Seattle, WA, USA) in a mobile monitoring campaign at a subset of 39 sites during the summer season.[155] In the study region, the concentrations of black carbon based on the particle light absorption coefficient are highly correlated with the concentrations of elemental carbon measured by traditional thermal/optical reflectance (R^2 = 0.7-0.8); 10^{-5}/m black carbon is approximately equivalent to 0.8 $\mu g/m^3$ elemental carbon.[158] Based on these measurements and after adjusting for temporal variation, we calculated annual average concentrations of these pollutants for each site.

Meanwhile, a total of 55 variables were generated in a Geographic Information System (GIS) (ArcGIS; ESRI, Redlands, CA, USA) to describe the land use characteristics of each site. Measured air pollutant concentrations and these predictive variables were modeled using multiple linear regression techniques, the most predictive variables were retained in the final model. As described previously,[40] we used the coefficient of determination (R^2) and estimated mean error from leave-one-

out cross-validation analysis to evaluate the performance of these models. Overall, the performance was similar to those of previous studies.[44] For NO [R^2 = 0.62, mean error ($\pm$ SD) = 2.02 $\pm$ 15.5 $\mu g/m^3$], the model included the length of highways within a 100-m and a 1000-m radius, the length of major roads within a 100-m radius, the population density within a 2500-m radius, around each sampling site, and the elevation of each site. For NO_2 (R^2 = 0.56, mean error = 0 $\pm$ 5.2 $\mu g/m^3$), the model included all variables in the NO model and also the area of commercial land within a 750-m radius. For $PM_{2.5}$ (R^2 = 0.52, mean error = 0 $\pm$ 1.50 $\mu g/m^3$), the model included the areas of commercial and industrial land within a 300-m radius, the area of residential land within a 750-m radius, and the elevation. For black carbon (R^2 = 0.56, mean error = 0 $\pm$ 0.23 $\times 10^{-5}$/m), the model included the length of major roads within a 100-m radius, distance to the nearest highway, and the area of industrial land within a 750-m radius. Overall, the performance (SD of mean error/sample mean) of the models for NO (10%), NO_2 (18%), and black carbon (14%) was better than that for $PM_{2.5}$ (36%).

Based on the LUR models, we generated a predicted spatial surface for annual average concentrations for each pollutant in a GIS with a resolution of 10 m. We then applied month-year adjustment factors derived from regulatory monitoring data to estimate monthly concentrations. The monthly air pollution data were assigned to subjects through their 6-digit residential postal codes (area centroids). In urban areas of metropolitan Vancouver, a 6-digit postal code represents one side of a city block, but may represent a larger area in less densely populated regions. After integrating changes in residences, we calculated average concentrations of black carbon, $PM_{2.5}$, NO_2, and NO during the 5-year exposure period, respectively, for each study subject.

Because the air pollution exposure assessment did not cover the whole study region, air pollution data were not available for a small proportion of study subjects. These subjects were thus

excluded from the analyses. Meanwhile, because of changes in residences, some subjects had partially missing air pollution data; those with missing data in more than a total of any 15 months or in more than 3 consecutive months during the 5-year exposure period were also excluded from the analyses.

3.2.4 Case Definitions

The outcomes of this study included CHD hospitalizations and CHD deaths that occurred during the 4-year follow-up period.

A CHD hospitalization case is a record of hospitalization with the following International Classification of Diseases (ICD) codes: ICD-9, 410-414 and 429.2 or ICD-10, I20-I25, as the principal diagnosis (the most responsible diagnosis) for a hospital admission in the provincial hospitalization database.

A CHD death is a death record with CHD as the cause of death in the provincial death registration database.

A broader definition was used to identify prior CHD cases. Subjects who had a hospitalization record with CHD as the principal or primary diagnosis (the diagnosis that had a substantial influence on hospital length of stay) before baseline (based on data from January 1991 to December 1998) were regarded as previously diagnosed CHD cases. These prior cases were excluded from the analysis to examine the association of incident CHD with traffic-related air pollution.

3.2.5 Covariates

We included age, sex, preexisting comorbidity, and neighborhood socioeconomic status (SES) as covariates in the data analysis. Preexisting comorbidity including diabetes[159] (ICD-9, 250; ICD-10, E10-E14), chronic obstructive pulmonary disease (COPD)[160] (ICD-9, 490-492 and 496; ICD-10, J40-J44), and hypertensive heart disease[159] (ICD9, 401-404; ICD10, I10-I13) are independent risk factors for CHD. In addition, these chronic diseases and CHD share common behavioral risk factors such as cigarette smoking. Given a lack of individual data on behavioral risk factors in this study, we used the preexisting comorbidity as a proxy variable of common behavioral risk factors.[163] To sufficiently control for the influence of the comorbidities and the common behavioral risk factors, all diagnoses in a hospitalization record (up to 16 diagnoses before 2001 and up to 25 diagnoses since 2001) were used to identify subjects with these comorbidities. One hospitalization record with the diagnosis of any of these diseases during January 1991 to December 1998 was defined as the presence of comorbidity.

Neighborhood SES reflects neighborhood disadvantages and is a risk factor for CHD.[168, 176] In addition, because individual SES data were not available in this study, we used neighborhood SES to approximate individual SES.[170, 171] The neighborhood-income quintiles from the 2001 Statistics Canada Census were assigned to study subjects using their residential postal codes. For the 2001 Census, a dissemination area with 400-700 persons was the smallest census unit for which all census data were disseminated. Within a census metropolitan area, all dissemination areas were ranked by household size-adjusted average family income and divided into quintiles.[174]

3.2.6 Statistical Analysis

The baseline characteristics between study subjects with different outcomes were compared using a *chi-square* test for categorical variables and *t* test for continuous variables. Correlations between these pollutants were examined using Spearman's rank correlation.

The Cox proportional hazards regression model was used to determine the associations of each air pollutant with CHD hospitalization and mortality. CHD hospitalization and CHD death were regarded as independent events; for CHD hospitalization analysis, CHD deaths without a hospitalization record were treated as censored cases like those who died from other diseases; for CHD mortality analysis, CHD hospitalization cases without a death record were treated the same way as those without a CHD event. Person-years were calculated for study subjects from baseline to the date of the first CHD hospitalization, CHD death, or end of follow-up. For those who died from other diseases or those who moved out of the province, person-years were calculated from baseline to the date of death or the last known date in the province. We first calculated relative risks (RRs) of CHD events in response to an interquartile range (IQR) elevation in the average concentration of each pollutant using bivariable and multivariable models. In the multivariable analysis, we gradually adjusted for age, sex, preexisting comorbidity, neighborhood income quintiles, and co-pollutants. We further examined exposure-response relationships by dividing study subjects into quintiles based on the concentrations of each pollutant. RRs of CHD events were calculated for quintile 2 to quintile 5 using quintile 1 (lowest) as the reference category. Linear trend across quintile groups was examined by using quintiles of a pollutant as a continuous variable.

For those pollutants associated with CHD hospitalization and mortality, we performed stratified analyses to examine effect modification by age, sex, preexisting comorbidity, and neighborhood SES. In this analysis, age was categorized into three groups (< 60, 60-69, ≥ 70 years)

as used in previous studies.[14, 16] Neighborhood SES was categorized into two groups: low (neighborhood income quintile 1-3) and high (neighborhood income quintile 4-5).

All statistical analyses were performed using SAS 9.2 software (SAS Institute Inc., Cary, NC, USA).

3.3 Results

At baseline, a total of 466,727 subjects who met the inclusion criteria were included in this study. Among these subjects, 13,992 (3.0%) with missing air pollution data were excluded, which left 452,735 subjects for the present analysis. During the 4-year follow-up period, 17,542 (3.9%) moved out of the province and 16,367 (3.6%) died from other diseases, leaving 418,826 (92.5%) subjects at the end of follow-up. Of these subjects, 45.9% were male; the average age (SD) was 58.9 (10.5) years (range, 45-83 years).

Although multiple ICD-9 and ICD-10 codes were used to identify CHD cases, acute myocardial infarction (ICD-9, 410 and ICD-10, I21 and I22) was the leading cause of hospitalization (41.2%) and death (56.8%). Compared with the subjects without CHD event, hospitalization cases and death cases were older and more likely to be male and have preexisting comorbidity and lower neighborhood SES, especially for death cases (Table 3.1).

Descriptive statistics and Spearman's rank correlation coefficients for these pollutants are summarized in Table 3.2. Overall, except for the correlation between NO_2 and NO, these pollutants were weakly correlated with each other.

3.3.1 Traffic-Related Air Pollution and CHD Hospitalization

During the follow-up period, 10,312 subjects were hospitalized for CHD (hospitalization rate, 6.0 per 1000 person-years). Exposure to black carbon was associated with CHD hospitalization. For an IQR elevation in black carbon concentration (0.94×10^{-5}/m), CHD hospitalization increased 4% [95% confidence interval (CI), 3-6%]. Adjusting for age, sex, preexisting comorbidity, and neighborhood SES reduced the effect estimate, whereas additional adjustment for co-pollutants ($PM_{2.5}$ and NO_2) increased the effect estimate (Table 3.3). $PM_{2.5}$ was similar to black carbon in the magnitude of association with CHD hospitalization, whereas NO_2 and NO were inversely associated with CHD hospitalization in adjusted models (Table 3.3).

CHD hospitalization gradually increased in response to quintiles of black carbon concentrations in bivariable and fully adjusted models, but not in the partially adjusted model (Figure 3.1A). In contrast, there was no linear exposure-response relationship between $PM_{2.5}$ and CHD hospitalization, and some evidence of inverse associations of NO_2 and NO with CHD hospitalization (Figure 3.1A).

Stratified analysis shows that CHD hospitalization in response to an IQR elevation in black carbon concentration was higher for people < 70 years of age and for those living in the areas with higher neighborhood SES (Figure 3.2A).

3.3.2 Traffic-Related Air Pollution and CHD Mortality

A total of 3,104 subjects died from CHD (mortality rate, 1.8 per 1000 person-years) during the follow-up period. Exposure to black carbon was strongly associated with CHD mortality. For an IQR elevation in black carbon concentration (0.94×10^{-5}/m), CHD mortality increased 14% (95% CI, 11-17%). Adjusting for age, sex, preexisting comorbidity, and neighborhood SES greatly reduced the

effect estimate; additional adjustment for co-pollutants ($PM_{2.5}$ and NO_2) did not change the effect estimate (Table 3.3). NO_2 and NO (but not $PM_{2.5}$) had a similar magnitude of association with CHD mortality.

There was also a strong exposure-response relationship between exposure to black carbon and CHD mortality in bivariable and multivariable models (Figure 3.1B). For NO_2 and NO, an exposure-response relationship was present in the bivariable models and in the multivariable models including age, sex, preexisting comorbidity, and neighborhood SES; but not after further adjusting for black carbon and $PM_{2.5}$ (Figure 3.1B). For $PM_{2.5}$, a linear trend was evident in the bivariable model but not in any of the adjusted models (Figure 3.1B).

Stratified analysis shows that CHD mortality associated with an IQR elevation in black carbon concentration was higher for men and for those 60-69 years of age, although there was considerable overlap in the risk estimates (Figure 3.2B).

During the 4-year follow-up period, there was no evident change in traffic-related air pollution such as $PM_{2.5}$ and NO_2 in this study region.[177] Our exposure assessment accounted for changes in residences during the exposure period. Further, a sensitivity analysis showed that the effect estimates remain unchanged after excluding those who changed their residences during the 4-year follow-up period.

3.4 Discussion

This large population-based cohort study demonstrated that long-term exposure to higher concentrations of black carbon was associated with increased risks of CHD hospitalization and mortality in an exposure-response fashion; the observed association with CHD mortality was particularly strong.

Black carbon results mainly from incomplete combustion of diesel fuels and is a surrogate for diesel exhaust particles.[29] It may also be emitted from other sources such as gasoline-powered vehicles and wood combustion.[29] Metropolitan Vancouver is a highly urbanized region, road traffic is the predominant source of black carbon and determines much of the spatial variability in the concentrations, especially during the summer season. In general, black carbon can be regarded as an indicator of the traffic-related component of fine particulate air pollution.[178, 179]

A recent case-control study used measured black carbon and NO_2 levels to estimate traffic particle levels and found that an IQR (0.2×10^{-5}/m) elevation in modeled traffic particle concentration was associated with a 10% (95% CI, 4-16%) increase in acute myocardial infarction.[180] In a 9-year Dutch cohort study, a 10 $\mu g/m^3$ increase in annual average concentration of black smoke was associated with a non-significant 4% increase in cardiovascular mortality.[74] A recent time-series study of 12 million Medicare enrollees in 119 US urban communities found that an IQR (0.4 $\mu g/m^3$) elevation in daily elemental carbon concentration was associated with a 0.8% (95% CI, 0.3-1.3%) increase in same-day cardiovascular hospitalizations. Elemental carbon was the only component of $PM_{2.5}$ that was associated with cardiovascular hospitalizations.[41] Similarly, in a time-series study, Laden el al[181] observed that traffic-related fine particles were more strongly associated with CHD mortality than with respiratory mortality, whereas coal-derived fine particles were more strongly associated with respiratory mortality than with CHD mortality. The findings of our study are consistent with those from previous studies, demonstrating that black carbon, as an indicator of traffic-related fine particulate air pollution, may be partly responsible for the observed associations between exposure to road traffic and adverse cardiovascular outcomes.

There is also strong evidence linking black carbon to various subclinical pathophysiological responses. Controlled exposure studies in healthy human volunteers demonstrated that short-term

exposure to diesel exhaust can cause acute artery vasoconstriction,[114] vascular endothelial dysfunction,[117, 118] and marked pulmonary and systemic inflammation.[118, 120, 121] Further, exposure to ambient black carbon or elemental carbon in $PM_{2.5}$ has been associated with airway[182] and systemic inflammation,[183] platelet activation,[183] plasma homocysteine,[184] heart rate variability,[179] cardiac arrhythmia,[185] and myocardial ischemia.[178, 186, 187] These findings suggest multiple biological mechanisms for the associations between black carbon and coronary events.

We did not find evidence of a linear exposure-response relationship between $PM_{2.5}$ and CHD hospitalization or mortality as reported in some previous studies.[14, 16] This finding was, however, consistent with the results of several other studies.[74, 83, 175] As mentioned before, in this study region, $PM_{2.5}$ levels were substantially lower in comparison with those of other metropolitan areas. In addition, road traffic was just one of numerous sources for ambient $PM_{2.5}$. Therefore the spatial distribution of $PM_{2.5}$ is relatively more homogeneous. The null exposure-response relationship between $PM_{2.5}$ and CHD probably reflects the inability of our exposure assessment method to differentiate spatial variability of $PM_{2.5}$ in this intraurban study.

Some studies have reported associations between long-term residential exposure to NO_2[35, 36] or NO_x[79] and CHD mortality. In these studies, NO_2/NO_x was used as a surrogate for within-city traffic-related air pollution. In our study, we also observed a linear exposure-response relationship between NO_2 or NO and CHD mortality. However, this relationship was mostly attenuated after adjusting for black carbon, suggesting that black carbon played a more important role than NO_2 and NO in association with CHD mortality in this study region.

This study has several strengths that support the validity of the findings. First, this large population-based cohort study included 452,735 subjects without known CHD at baseline. The large sample size and statistical power enabled this study to detect small adverse coronary effects with

relatively higher precision. Second, this study used two different coronary outcomes, hospitalization and mortality (from different data sources), to evaluate the adverse effects of these air pollutants; the associations between black carbon and these two outcomes were consistent. Third, we collected detailed residential history information. Average concentrations of air pollutants were calculated for each subject after integrating changes in residences during the 5-year exposure period. As previously demonstrated,[174] this method can effectively reduce exposure misclassification from residence relocation. Fourth, we used LUR models with high spatial resolution for exposure assessment. This approach facilitates spatial variability of pollutant concentrations and provides increased exposure contrasts and statistical power.

This study also has some limitations. First, the cohort was constructed using provincial health insurance registry and linked administrative health databases. As previously discussed,[174] some important information about individual cardiovascular risk factors such as cigarette smoking was not available and thus could not be controlled in data analysis. We adjusted for age, sex, preexisting comorbidity (diabetes, COPD, hypertensive heart disease), and neighborhood socioeconomic status. Because these comorbidities and CHD share common behavioral risk factors, adjusting for these comorbidities to some extent was able to reduce the influence of some uncontrolled risk factors and these comorbidities themselves on the effect estimates.[163] On the other hand, because diabetes, COPD, and hypertensive heart disease might serve as intermediate variables for the association between traffic-related air pollution and coronary events, adjusting for these comorbidities might lead to underestimations of the true adverse effects.[188]

Second, cigarette smoking is the single most important risk factor for CHD and was not measured in this study.[164] However, previous studies have shown that cigarette smoking did not substantially affect the associations between fine particulate air pollution and adverse cardiovascular

outcomes such as coronary atherosclerosis,[83] carotid intima-media thickness,[84] and CHD mortality.[70] Based on these previous findings, we believe that the observed associations in this study are unlikely to be due to the confounding effects of cigarette smoking.

Third, low individual SES is a risk factor for CHD[165] and may be also related to exposure to traffic-related air pollution.[169] Individual SES is thus a possible confounder for the observed association. As mentioned before, because individual SES was not available in this study, we used neighborhood income quintiles to approximately estimate individual SES. There is some evidence that this approach is valid for control of individual SES;[170, 171] however, this approach was unlikely to control all confounding effects related to individual SES.[189]

Fourth, like those used in previous studies, the exposure assessment in this study can only approximately reflect the exposure levels at subjects' residences (postal code centroids). Many factors such as air infiltration, individual mobility, and outdoor activity might substantially affect actual individual exposure to traffic-related air pollution. This exposure assessment method did not take into account these individual factors and thus cannot precisely reflect actual individual exposure levels. Nevertheless, these factors are most likely to cause non-differential exposure misclassification, leading to underestimations of the true adverse coronary effects.[190]

Fifth, exposure to traffic-related air pollution may be associated with exposure to traffic noise.[61] Some evidence has indicated that exposure to traffic noise is associated with CHD events.[22] In the present study, traffic noise might also play a role in the association between black carbon and CHD events.

Sixth, because of privacy protection, we were unable to contact CHD cases or access their original medical records. As a result, we were unable to evaluate the accuracy of CHD diagnosis recorded in the provincial hospitalization database and death registration database. There were up to

16 diagnoses (1991-2000) or up to 25 diagnoses (2001-2002) in each hospitalization record. To reduce the possibility of misdiagnosis, we used only the principal diagnosis (the most responsible diagnosis for a hospital admission) to identify hospitalization cases. This stringent definition for hospitalization case might improve the accuracy of the CHD classification; however, we might inevitably lose some hospitalization cases for which CHD was not the principal diagnosis and thereby underestimate the true adverse effects.

Finally, although air pollution exposures were estimated based on residential postal codes, because of privacy protection, residential postal codes were eliminated from data files after data linkage. Therefore, we were unable to access residential postal codes of subjects and cannot adjust for spatial clustering of the air pollution data, which might lead to underestimations of the standard errors in Cox regression models.

In conclusion, this large population-based cohort study demonstrated that long-term exposure to higher concentrations of black carbon was associated with an increased risk of CHD hospitalization and mortality in an exposure-response fashion. These findings suggest that traffic-related fine particulate air pollution, indicated by black carbon, may be partly responsible for the observed associations between exposure to road traffic and adverse cardiovascular outcomes.

Table 3.1 Baseline Characteristics of Study Subjects

Covariate	Subjects Without CHD Event (n = 406,232)	Hospitalization Cases[a] (n = 10,312)	Mortality Cases[a] (n = 3,104)
Men (%)	45.3	66.4	61.5
Age (SD) (years)	58.7 (10.4)	65.4 (10.1)	72.5 (8.9)
Comorbidity (%)			
Diabetes	1.8	7.9	13.3
COPD	1.0	2.8	9.8
Hypertensive heart disease	3.6	10.8	19.3
Any of the above	5.5	17.2	31.2
Income quintiles (%)[b]			
1	17.9	19.8	26.2
2	18.9	19.5	21.6
3	19.5	19.4	18.3
4	20.7	20.7	18.1
5	23.1	20.5	15.8

Abbreviations: CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease.

[a] $P < 0.05$ for all comparisons with subjects without CHD event.

[b] Quintile 1 represents the lowest, quintile 5 the highest neighborhood income quintile.

Table 3.2 Average Concentrations of Traffic-Related Air Pollutants during the Exposure Period and Correlation Coefficients

Pollutant	Mean ± SD	Median	IQR	Range	Correlation Coefficient[a]			
					BC	$PM_{2.5}$	NO_2	NO
BC (10^{-5}/m)	1.49 ± 1.10[b]	1.02	0.94	0-4.98	1.00	--	--	--
$PM_{2.5}$ (μg/m^3)	4.08 ± 1.63	4.03	1.58	0-10.24	0.13	1.00	--	--
NO_2 (μg/m^3)	32.1 ± 8.0	30.6	8.4	15.3-57.7	0.39	0.47	1.00	--
NO (μg/m^3)	32.0 ± 11.9	29.3	13.2	8.8-126.0	0.42	0.43	0.67	1.00

Abbreviations: BC, black carbon; IQR, interquartile range.

[a] $P < 0.001$ for each correlation coefficient.

[b] Equivalent to approximately 1.19 ± 0.88 μg/m^3 elemental carbon (10^{-5}/m black carbon ≈ 0.8 μg/m^3 elemental carbon).

Table 3.3 RRs (95% CIs) of Coronary Heart Disease Hospitalization and Mortality for an Interquartile Range Elevation in Average Concentrations of Traffic-Related Air Pollutants

Model	BC (0.94×10^{-5}/m)[a]	$PM_{2.5}$ (1.58 μg/m^3)[a]	NO_2 (8.4 μg/m^3)[a]	NO (13.2 μg/m^3)[a]
Hospitalization				
(1) Unadjusted single pollutant	1.04 (1.03-1.06)	1.03 (1.01-1.05)	1.02 (1.00-1.04)	0.99 (0.97-1.02)
(2) Model (1) + sex, age, comorbidity, SES	1.01 (1.00-1.03)	1.00 (0.98-1.02)	0.97 (0.95-0.99)	0.96 (0.94-0.98)
(3) Model (2) + 2 other pollutants[b]	1.03 (1.01-1.05)	1.02 (1.00-1.05)	0.96 (0.94-0.98)	0.95 (0.92-0.97)
Mortality				
(1) Unadjusted single pollutant	1.14 (1.11-1.17)	1.13 (1.09-1.16)	1.19 (1.15-1.23)	1.13 (1.09-1.17)
(2) Model (1) + sex, age, comorbidity, SES	1.06 (1.03-1.09)	1.01 (0.98-1.05)	1.04 (1.01-1.08)	1.06 (1.02-1.10)
(3) Model (2) + 2 other pollutants[b]	1.06 (1.03-1.09)	1.00 (0.96-1.03)	1.03 (0.99-1.07)	1.03 (0.99-1.08)

Abbreviations: BC, black carbon; SES, neighborhood socioeconomic status.

[a] Interquartile range.

[b] Additionally adjusted for $PM_{2.5}$ and NO_2 for black carbon, black carbon and NO_2 for $PM_{2.5}$, black carbon and $PM_{2.5}$ for NO_2 and NO.

Figure 3.1 RRs and 95% CIs of CHD Hospitalization (A) and Mortality (B) by Quintiles of Black Carbon Concentrations

Quintile 1 was the reference category. From the left to right, each error-bar represents RR and 95% CI of CHD hospitalization (A) or mortality (B) for quintile 2-5, respectively, compared with quintile 1(lowest). P_{trend} indicates linear trend across quintile groups.

Model 1, bivariable analysis; Model 2, adjusted for age, sex, preexisting comorbidity, and neighborhood SES; Model 3, additionally adjusted for co-pollutants $PM_{2.5}$ and NO_2.

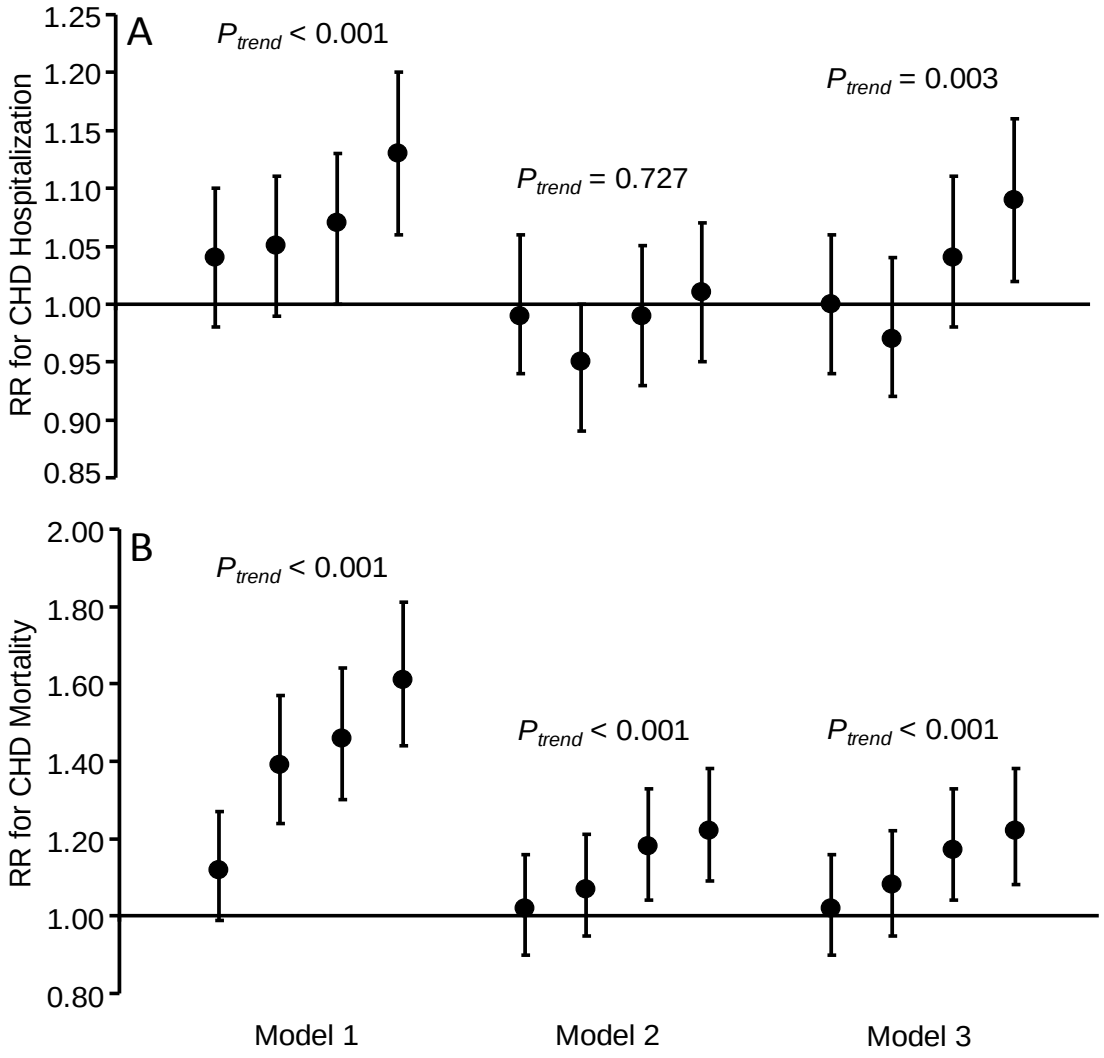
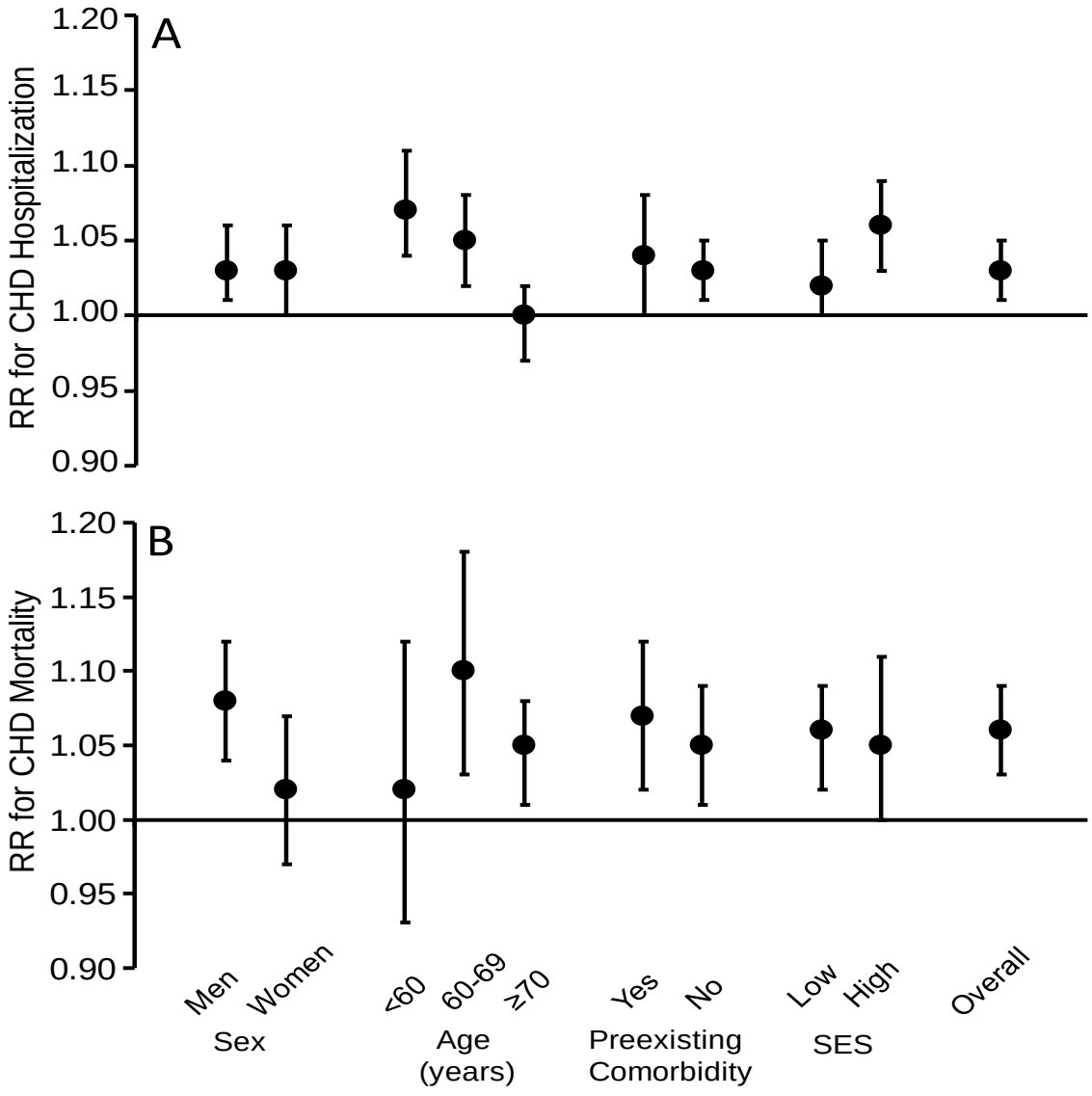


Figure 3.2 Adjusted RRs and 95% CIs for CHD Hospitalization (A) and Mortality (B) Associated with an IQR Elevation in Black Carbon Concentration

Stratified by Each Covariate and Adjusted for All Other Covariates in the Figure and Copollutants Including $PM_{2.5}$ and NO_2



Chapter 4: Modeling Population Exposure to Community Noise and Air Pollution in a Large Metropolitan Area

4.1 Introduction

Long-term exposure to excessive community noise including road traffic noise, aircraft noise, and railway noise has been associated with annoyance, sleep disturbance, psychological stress, and cardiovascular disease.[25, 27, 148] In the European Union, approximately 40% of the population is exposed to residential noise levels above 55 dB(A) during daytime and more than 30% is exposed to the same noise levels at night; this exposure may cause annoyance and sleep disturbance.[25] Worldwide, because of rapid urbanization, community noise has been increasingly regarded as an important public health problem.[25, 27, 148] In the European Union, all Member States are required to produce strategic noise maps for large urban areas with over 250,000 population.[87] However, in North America, there is little information about community noise exposure in large metropolitan areas.

To better understand adverse health effects associated with exposure to community noise, accurate exposure assessment is critical. In large-scale long-term epidemiologic studies, personal noise exposure sampling or community noise monitoring is not feasible because noise levels can be highly variable and infrequent field measurements are unlikely to collect representative noise exposure samples for large numbers of study participants. Instead, noise prediction models are widely used to estimate residential exposure to community noise.[87] With few exceptions,[191-193] almost all epidemiologic studies on the relationships between community noise and cardiovascular diseases used prediction models for noise exposure assessment.[19-23, 89, 96, 194, 195] In this paper, our

primary purpose was to describe a model-based noise exposure assessment used in a large population-based cohort study to examine the relationships between exposure to community noise, traffic-related air pollution, and cardiovascular disease mortality in metropolitan Vancouver, Canada.

Furthermore, epidemiologic studies have shown that both community noise and air pollution are associated with cardiovascular disease morbidity and mortality.[11, 21, 22] In metropolitan areas, road traffic is a major contributor to ambient air pollution, and also the dominant source of community noise.[61, 62, 196, 197] People exposed to excessive noise may also be exposed to higher levels of traffic-related air pollution. Therefore, a major concern in epidemiologic studies of associations between cardiovascular diseases and community noise or traffic-related air pollution is that the observed associations may be confounded by coexistent traffic-related pollutants.[11, 61, 62, 196, 197] To address this concern, the secondary purpose of this paper was to investigate correlations between community noise and traffic-related air pollution. Based on the correlation levels, we could evaluate the potential confounding effects and determine whether it was feasible to control for the confounding effects in epidemiologic studies.[61, 62, 196, 197]

4.2 Methods

The study region, metropolitan Vancouver, located on the west coast of Canada, covers approximately 2000 km^2 and comprises 22 municipalities (the largest being the cities of Vancouver, Surrey, and Richmond), with a population of 2.1 million in 2003. In this region, community noise mainly comes from road traffic, aircraft, and railways, with road traffic as the dominant noise source.[198] Road traffic is also a major contributor to ambient air pollution, responsible for most of the spatial variability in traffic-related air pollution in this region.[154, 155]

4.2.1 Noise Exposure Assessment

Noise prediction models have been widely used worldwide, especially in the European Union, to estimate community noise exposure and predict the influence of new facilities or noise abatement programs.[87, 88, 199, 200] Noise prediction models estimate community noise exposure through quantitative analysis of the generation (e.g. road traffic), propagation (e.g. topographical effects, atmospheric absorption), and attenuation (e.g. screening effects and buildings reflections) of various noise sources.[88] There are many noise prediction models worldwide; in general, these models are similar in calculation and accuracy.[88, 200, 201] We used CadnaA (Computer Aided Noise Abatement), a model-based computer program developed by DataKustik (Greifenberg, Germany), to estimate annual average community noise levels for the year 2003 based on the following input data.

4.2.1.1 Road Traffic Noise

Traffic volume: Traffic volume data were not available for most municipalities in the study region. Therefore, a 2003 transportation planning model EMME/2 (INRO Consultants, Montreal, Canada) from the Metro Vancouver transportation authority was used to estimate average daily traffic volumes. This method is widely used in large-scale noise mapping.[202, 203]

Road width: road width data were not available; therefore the distance between the centerlines of the outer lanes was used to estimate the road width. For one-lane roads, based on our actual measurements in the study region, an average width of 4 m was entered.

Road type: Based on the provincial Digital Road Atlas,[152] road type was divided into three categories (corresponding road type in CadnaA): freeway (motorway); highway, arterial, or collector (ordinary road); and local (local road). Each road type was automatically assigned a specific percentage of trucks (maximum weight >2.8 tons).

In addition, the model also took into account the influence of road speed limits, traffic lights at intersections, road gradient (change in elevation along a given road), road surface (paved or loose surface), bridges (heights of the road segments above ground), buildings (height, footprint, and reflection/absorption characteristics), and topography in the exposure assessment of road traffic noise. For each municipality in metropolitan Vancouver, the data for each traffic attribute were available to a different degree and in different quality.

We used GIS Innovations (Tallahassee, Florida, USA) and other available data sources including municipal traffic counts, Google Earth, and a Geographic Information System (GIS) (ArcGIS; ESRI, Redlands, CA, USA) to retrieve these road traffic data. The data were entered in accordance with the German guidelines for road traffic noise prediction (German Standard RLS-90).[204]

4.2.1.2 Aircraft Noise

Vancouver International Airport is the second busiest airport in Canada, and also the dominant source of aircraft noise in the study region. The Airport Authority produces aircraft noise exposure forecast contours to describe the noise exposure levels in the area surrounding the airport.[205] The noise contours are created using noise prediction models that take into account aircraft operation information including flight path, frequency, aircraft types, and local meteorology. We used the noise exposure forecast contours for 2003 to estimate aircraft noise levels in the area around the airport.

4.2.1.3 Railway Noise

In the study region, the urban rapid transit system ("skytrain") is the major railway noise source. Railway noise exposure assessment was based on railway operation data including length of trains, velocity, percentage of disk brakes, and number of each type of train by day, evening, and night. The German railway guideline (Schall-03, edition 1990) was used for railway noise assessment.

4.2.1.4 Noise Modeling

Based on the above data, annual day-evening-night A-weighted equivalent continuous noise levels (L_{den} dB(A)) were calculated for a 10 × 10 m grid of receivers 4 m above the ground. The L_{den} metric integrates noise levels during the day (L_{day}, 6:00 am - 18:00 pm), the evening (18:00 pm - 22:00 pm), and the night (L_{night}, 22:00 pm - 6:00 am); it reflects increased sensitivity of residents to community noise at evening and night by adding a 5 dB(A) weighting to evening noise levels and a 10 dB(A) weighting to night noise levels.[27] Based on the estimated noise levels for these grids, annual average noise levels for (1) all sources, (2) road traffic only, and (3) aircraft only were calculated, respectively, for each area covered by a 6-digit postal code. Study subjects were then assigned noise exposure data based on their residential postal codes. In the study region, postal code areas vary greatly in size dependent on the density of population: in urban areas, a postal code typically represents a high-rise building or one side of a city block; however, in rural areas, a postal code may represent a larger area. Because metropolitan Vancouver is a highly urbanized region, the vast majority of the postal codes represent small geographical areas. On average, a residential postal code may include about 35 persons.

4.2.1.5 Short-Term Noise Exposure Sampling

As described in detail in a previous study,[61] Davies and colleagues measured 5-min daytime A-weighted equivalent continuous noise levels ($L_{eq,day,5\ min}$) at 103 selected sites in the study region. These sites were selected using a location-allocation model to maximally describe the variability of traffic-related air pollution in this region.[154] Noise measurement was performed during the period of air pollution sampling (daytime from 8:00 am to 18:00 pm) using LDL 870 Environmental Noise Analyser (Larson Davis, Provo, Utah, USA) and LDL 2559 microphone, which was placed 1.2 m above the ground with a 90° angle. Calibration was performed with a B&K 4231 calibrator (Bruel & Kjaer, Naerum, Denmark) each morning before sampling.[61] We used the measured short-term noise exposure data to evaluate the performance of the noise prediction model.

4.2.2 Air Pollution Exposure Assessment

We used a high-resolution land use regression (LUR) model to estimate traffic-related air pollutant concentrations for each postal code area in the study region in 2003. This method has been described in detail elsewhere.[40, 154, 155] In brief, the concentrations of black carbon, $PM_{2.5}$, NO_2 and NO were measured in selected sampling sites, respectively. Based on these measurements and adjustment for temporal variation, annual average concentrations of these pollutants were calculated for each site. Meanwhile, a total of 55 variables were generated in a GIS to describe the land use characteristics of each site that might potentially predict the concentrations of these air pollutants. Then multiple linear regression techniques were used to describe the quantitative relationships between measured air pollutant concentrations and the selected land use characteristics, and those most predictive variables were retained in the final models. The coefficient of determination (R^2) was used to evaluate the performance of these models. For NO (R^2 = 0.62), the model included the length

of highways within a 100-m and a 1,000-m radius, the length of major roads within a 100-m radius, the population density within a 2,500-m radius, around each sampling site, and the elevation of each site. For NO_2 (R^2 = 0.56), the model included all variables in the NO model and also the area of commercial land within a 750-m radius. For $PM_{2.5}$ (R^2 = 0.52), the model included the areas of commercial and industrial land within a 300-m radius, the area of residential land within a 750-m radius, and the elevation. For black carbon (R^2 = 0.56), the model included the length of major roads within a 100-m radius, the distance to the nearest highway, and the area of industrial land within a 750-m radius. Based on the LUR models, a smooth spatial surface of predicted annual average concentrations for each air pollutant was generated in a GIS with a resolution of 10 m. Annual average concentrations of these air pollutants were assigned to each postal code in the study region.

4.2.3 Statistical Analysis

We performed correlation analysis for modeled and measured noise levels at the 103 selected sites. Because a high correlation does not necessarily imply that there was good agreement between the two measurements, we also used a Bland-Altman plot to examine their agreement in which the differences between the two measurements are plotted against the averages of the two measurements. Further, we divided modeled and measured noise levels into tertile groups (low, medium, high), respectively, and examined the degree of agreement between these two ordinal categorical variables using a linear weighted kappa coefficient, which takes into account not only the absolute concordances but also the relative concordances (the closeness of a rank to the correct rank).

Because the distribution of black carbon was right skewed, we used Spearman's rank correlation coefficient (r) to evaluate the correlation between noise and black carbon. For other air pollutants, the distributions were close to normal, and Pearson's correlation and Spearman's rank

correlation analyses yielded similar results. For consistency, we used Spearman's rank correlation coefficient to evaluate the correlations between noise and each air pollutant. In addition, to compare the correlation levels across areas with different noise levels, we divided postal code areas into tertile groups based on modeled noise levels, representing low, medium, and high levels of noise exposure, and calculated the correlations for each tertile group.

The analyses were performed with SAS 9.2 and S-Plus 8.0.

4.3 Results

There were 59,326 postal codes in the study region. On average, the modeled L_{den} was 64 [inter-quartile range (IQR), 60-68] dB(A), L_{day} was higher than L_{night} [64 (IQR, 60-68) vs. 54 (IQR, 50-58) dB(A)], and road traffic noise level (L_{den}) was higher than aircraft noise level [63 (IQR, 59-67) vs. 32 (IQR, 22-44) dB(A)] (Table 4.1). Descriptive statistics for modeled noise levels and modeled concentrations of traffic-related air pollutants including black carbon, $PM_{2.5}$, NO_2, and NO are summarized in Table 4.1. The noise exposure across the central area of the study region is presented in Figure 4.1.

Because short-term noise exposure sampling was performed during daytime (8:00 am to 18:00 pm) at the 103 sites, we used modeled daytime noise levels (L_{day}) at the 103 sites to evaluate the performance of the model. For the 103 selected sites, the average noise level was 68 (median, 65) dB(A) based on the prediction model (L_{day}), and 62 (median, 60) dB(A) based on field sampling ($L_{eq,day,5\ min}$). On average, L_{day} was 6.2 (95% CI, 6.0-7.9) dB(A) higher than $L_{eq,day,5\ min}$. The Bland-Altman plot shows that L_{day} was higher than $L_{eq,day,5\ min}$ in most of the selected sites but does not show a strong dependence of the agreement between two measurements on the noise levels (Figure 4.2). However, these two measurements were highly correlated ($r = 0.62$, $P < 0.001$)

(Figure 4.3). When both modeled and measured noise levels were treated as tertile groups, the agreement between these two measurements is acceptable (weighted kappa coefficient, 0.41; 95% CI, 0.28-0.54).

The correlations between community noise and traffic-related air pollutants range from 0.18 to 0.48 (Table 4.2); noise levels were more strongly and consistently correlated with black carbon concentrations (r = 0.48), and weakly correlated with $PM_{2.5}$ concentrations (r = 0.18). For black carbon and NO, the correlation levels were gradually elevated across the tertiles of noise levels; but no such trend was observed for $PM_{2.5}$ or NO_2 (Table 4.2).

Table 4.3 shows the correlations between noise and air pollutants stratified by traffic proximity. The correlations tended to be higher for postal code areas farther than 50 m or 150 m from highways (21,000-114,000 vehicles/day). For major roads (15,000-18,000 vehicles/day), there was no consistent effect of traffic proximity on the correlations (Table 4.3).

Overall, aircraft noise levels were inversely correlated with black carbon concentrations (r = -0.07, $P < 0.001$), particularly at the medium range of aircraft noise levels (26 - 41 dB(A)). An inverse correlation between aircraft noise and NO_2 or NO was also present (Table 4.4). There was no consistent effect of aircraft or road traffic noise levels on the correlations with traffic-related air pollutant concentrations (Table 4.4).

4.4 Discussion

We used a noise prediction model to assess long-term exposure to community noise in a large metropolitan area. On average, modeled annual average noise level was 64 dB(A) for all sources and 63 dB(A) for road traffic. The modeled road traffic noise level was higher than that in European cities such as the Netherlands (L_{den}, 52 dB(A)).[89] Although our noise prediction model tended to

overestimate the actual noise exposure, the modeled daytime noise levels were highly correlated with measured short-term noise levels (r = 0.62), suggesting that the model-based noise exposure assessment could approximately reflect actual noise exposure in the study region.

We used 5-min equivalent continuous noise levels at 103 selected sites to evaluate the accuracy of the model-based noise exposure assessment. There is some evidence that short-term noise levels may be a good indicator of long-term noise levels;[61, 62] however, these "grab samples" can only serve as crude approximations for long-term noise levels because noise levels may vary greatly from time to time in urban environment.

Our analyses show that overall modeled noise levels were not strongly correlated in space with traffic-related air pollutant concentrations: the highest correlation was with black carbon (r = 0.48), the lowest correlation was with $PM_{2.5}$ (r = 0.18). To some extent, the findings reflect the fact that black carbon, an indicator of traffic-related fine particulate pollution,[178, 179] is mainly derived from road traffic, whereas $PM_{2.5}$ may come from various sources including motor vehicles, as well as various regional sources and secondary production.[154, 155, 177] In this study, the correlation of modeled annual average noise levels with modeled annual average concentrations of NO_2 and NO was 0.38 and 0.45, respectively. We previously found that measured short-term noise levels ($L_{eq,day,5\ min}$) were moderately correlated with measured 2-week average concentrations of NO_2 (r = 0.53) and NO (r = 0.64) in the study region.[61] Using a similar method, Allen et al found that the correlation of $L_{eq,day,5\ min}$ with 2-week average concentrations of NO was from 0.20 to 0.60 in two US cities Chicago and Riverside County.[62] Foraster et al found that the correlation between modeled $L_{eq,24h}$ and measured annual average concentrations of NO_2 was 0.62 in Girona, Spain; but notably the correlations varied substantially from 0.39 to 0.87 across different locations in the city.[196] There are also several other studies that examined the correlations of community noise with various air pollutants (NO_2, NO_x,

PM_{10}, black smoke) using different methods (sampling or modeling) and durations (from day to year).[22, 89, 96, 99, 206, 207] Overall, the reported correlation levels vary substantially across different geographic regions and even across different locations within the same regions. In addition to the differences in specific air pollutants and exposure assessment methods, numerous other factors such as traffic attributes (e.g. speed, volume, and composition), population density, degree of urbanization, meteorological factors (e.g. wind direction and speed), and topographic factors may also contribute to the differences in the correlations.

This study shows that the correlations between community noise and traffic-related air pollutants (e.g. $PM_{2.5}$ and NO_2) were not necessarily linear and areas near major roadways might not necessarily have higher correlations. Allen et al also did not find a consistent influence of traffic proximity on correlations between road traffic noise and NO or NO_2.[62] Foraster et al reported that the correlations were lower in areas with higher traffic density, but higher in areas with lower traffic density.[196] These results are plausible because many environmental factors may differentially affect noise levels and traffic-related air pollutant concentrations.[88, 208, 209] First, traffic-related air pollution and noise emissions vary greatly in response to changes in vehicle speed. For example, when vehicle speed is less than 30 km/h during traffic congestion, noise emissions are lower; but air pollution emissions are relatively higher. When vehicle speed is over 40 km/h, noise emissions, mainly from tire-road interaction, are rapidly increased; but air pollution emissions are relatively lower.[88, 209] Second, traffic-related air pollution is strongly dependent on traffic volume (traffic intensity); but traffic volume has a smaller influence on traffic noise. For example, when traffic volume doubles, traffic noise levels increase only 3 dB(A).[88] Third, meteorological factors such as wind direction and speed may strongly influence the concentrations of traffic-related air pollution, but have smaller influence on traffic noise level. As a result, correlations for downwind areas of major roadways are

higher than those of upwind areas.[62] In addition, rain and wet road surface may substantially increase road traffic noise levels; but may substantially reduce ambient air pollutant concentrations. Finally, some factors such as surrounding buildings and road pavement materials have strong influence on traffic noise levels, especially when vehicle speed is over 40 km/h; but have little influence on air pollution concentrations.[88] These factors may partly explain the low-to-moderate correlations between community noise and traffic-related air pollution. Our results suggest that it is possible to take into account both community noise and traffic-related air pollution in epidemiologic studies concerning traffic-related pollution and adverse cardiovascular outcomes.[61, 62, 196, 197]

There are some limitations for our noise exposure assessment. First of all, the accuracy of model-based noise exposure assessment was dependent on the availability of raw data for various transportation attributes.[210] In some areas of metropolitan Vancouver, required data such as road traffic volume data and surrounding building data were not available. For example, we used the distance between the centerlines of the outer lanes to estimate the road width and used the transportation planning model EMME/2 to estimate average daily traffic volumes. Although the methods are widely used in large-scale noise mapping,[202] these approximate data and some missing data might introduce measurement error. In addition, there were no transportation noise modeling guidelines in Canada, we used the German road (RLS-90) and railway (Schall-03) noise prediction guidelines. Some default parameters such as the percentage of trucks for each road type, based on German road traffic, were therefore assigned in the noise modeling. Although previous studies have demonstrated that the German noise guidelines could be used in other geographical areas,[196, 201, 211, 212] it is necessary to develop transportation noise guidelines that are specific for the study region.

In conclusion, we used a noise prediction model to assess community noise levels in a large metropolitan area. Although our noise prediction model tended to overestimate the actual noise

exposure, the modeled daytime annual average noise levels were highly correlated with measured short-term noise levels, suggesting that the model-based noise exposure assessment could approximately reflect actual noise exposure in the study region.

Overall, community noise levels were not strongly correlated with traffic-related air pollutant concentrations. There was not a consistent effect of noise levels or traffic proximity on the correlations between community noise and traffic-related air pollutant concentrations. Our analyses suggest that it is feasible to take into account both community noise and traffic-related air pollution in epidemiologic studies concerning traffic-related pollution and adverse cardiovascular outcomes in this study region.

Table 4.1 Noise Levels and Air Pollutant Concentrations

Pollutant	Mean ± SD	Median	IQR
Noise			
L_{den} (dB(A))	63.8 ± 6.0	62.6	59.8 - 67.6
L_{day} (dB(A))	64.3 ± 5.9	63.1	60.3 - 68.1
L_{night} (dB(A))	53.8 ± 5.9	52.6	49.9 - 57.5
Road Traffic, L_{den} (dB(A))	63.1 ± 5.9	61.9	59.2 - 66.8
Aircraft, L_{den} (dB(A))	32.1 ± 16.2	34.8	22.3 - 43.9
Air Pollutants			
BC (10^{-5}/m)[a]	1.71 ± 1.35	1.01	0.85 - 2.15
$PM_{2.5}$ ($\mu g/m^3$)	4.06 ± 1.73	4.01	3.14 - 4.78
NO_2 ($\mu g/m^3$)	31.4 ± 8.3	29.5	26.0 - 34.0
NO ($\mu g/m^3$)	32.8 ± 15.6	28.5	23.3 - 37.4

Abbreviations: BC, black carbon; IQR, interquartile range; L_{day} dB(A), annual daytime A-weighted equivalent continuous noise level; L_{den} dB(A), annual day-evening-night A-weighted equivalent continuous noise level; L_{night} dB(A), annual nighttime A-weighted equivalent continuous noise level; SD, standard deviation.

[a] Equivalent to approximately 1.37 ± 1.08 $\mu g/m^3$ elemental carbon (10^{-5}/m black carbon ≈ 0.8 $\mu g/m^3$ elemental carbon).

Table 4.2 Correlations between Noise and Traffic-Related Air Pollutants

Air Pollutant	Tertiles of Noise Levels (dB(A))			Overall
	Low (≤ 61)	Medium (62-66)	High (> 66)	
BC	0.08	0.20	0.35	0.48
$PM_{2.5}$	0.20	-0.02	0.12	0.18
NO_2	0.20	0.07	0.27	0.38
NO	0.12	0.14	0.38	0.45

Abbreviations: BC, black carbon; dB(A), A-weighted decibels

Table 4.3 Correlations between Noise and Traffic-Related Air Pollutants by Traffic Proximity

Road Proximity[a]	Number	BC	$PM_{2.5}$	NO_2	NO
≤ 50 m Highway	2262	0.17	0.02	0.04	0.14
> 50 m Highway	57,064	0.45	0.17	0.36	0.42
≤ 150 m Highway	6157	0.38	0.03	0.23	0.35
> 150 m Highway	53,169	0.41	0.17	0.35	0.40
≤ 50 m Major Road	8602	0.26	0.24	0.38	0.37
> 50 m Major Road	50,724	0.41	0.16	0.32	0.33
≤ 150 m Major Road	25,113	0.46	0.15	0.30	0.47
> 150 m Major Road	34,213	0.31	0.14	0.26	0.22
Total	59,326	0.48	0.18	0.38	0.45

Abbreviations: BC, black carbon.

[a] Highways: 21,000-114,000 vehicles per day; major roads: 15,000-18,000 vehicles per day.

Table 4.4 Correlations of Noise from Road Traffic and Aircraft with Traffic-Related Air Pollutants

Air Pollutant	Tertiles of Noise Levels			Overall
	Low	Medium	High	
Road traffic noise				
BC	0.03	0.19	0.33	0.45
$PM_{2.5}$	0.15	-0.01[a]	0.11	0.14
NO_2	0.10	0.07	0.26	0.33
NO	0.06	0.13	0.36	0.41
Aircraft noise				
BC	0.14	-0.24	0.16	-0.07
$PM_{2.5}$	0.10	-0.01[a]	0.33	0.31
NO_2	0.02	-0.13	0.06	0.14
NO	0.22	-0.14	0.27	0.26

Abbreviations: BC, black carbon.

[a] $P > 0.05$

Figure 4.1 Noise Map for Central Area of Metropolitan Vancouver in 2003

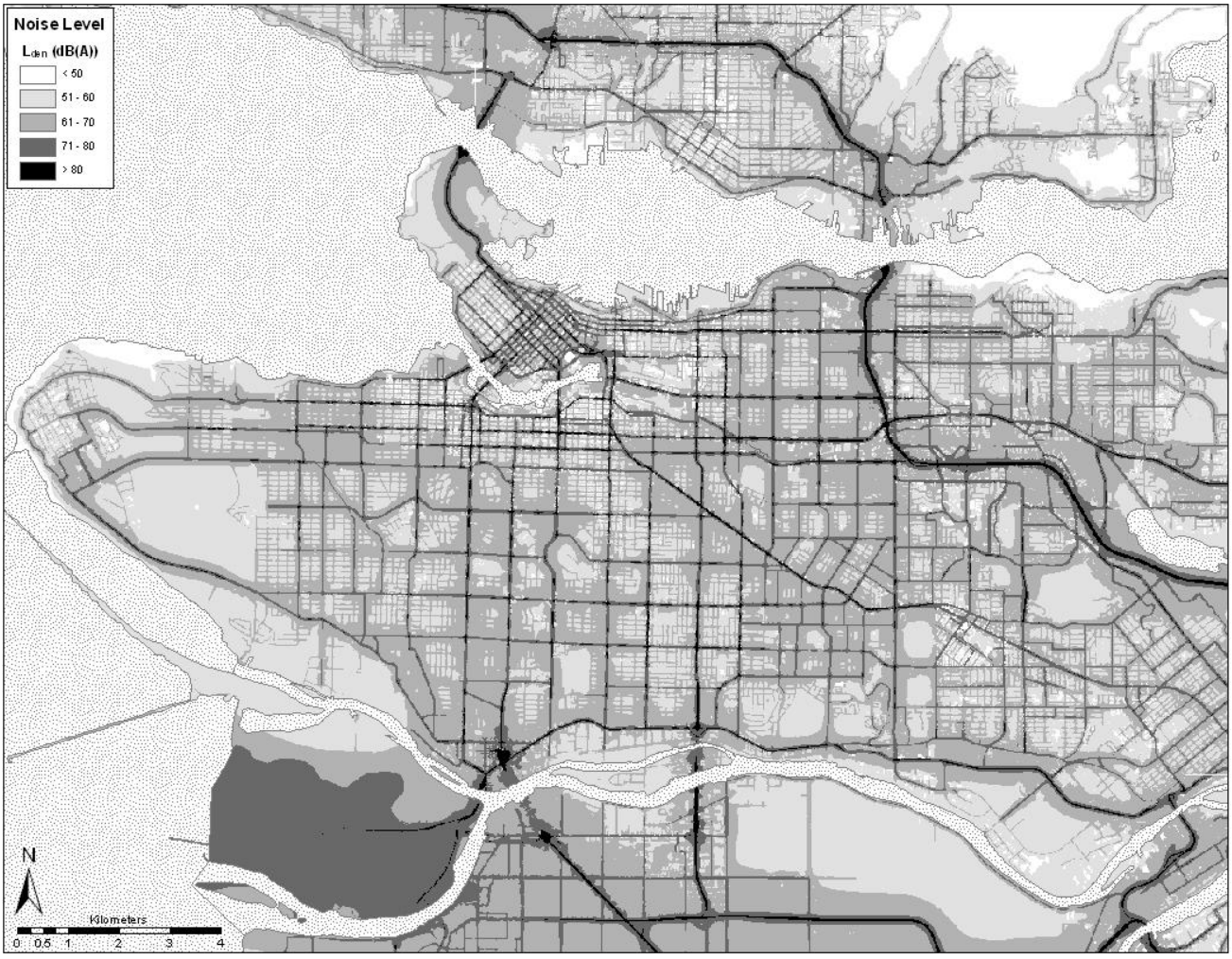


Figure 4.2 Bland-Altman Plot Comparing Modeled and Measured Noise Levels

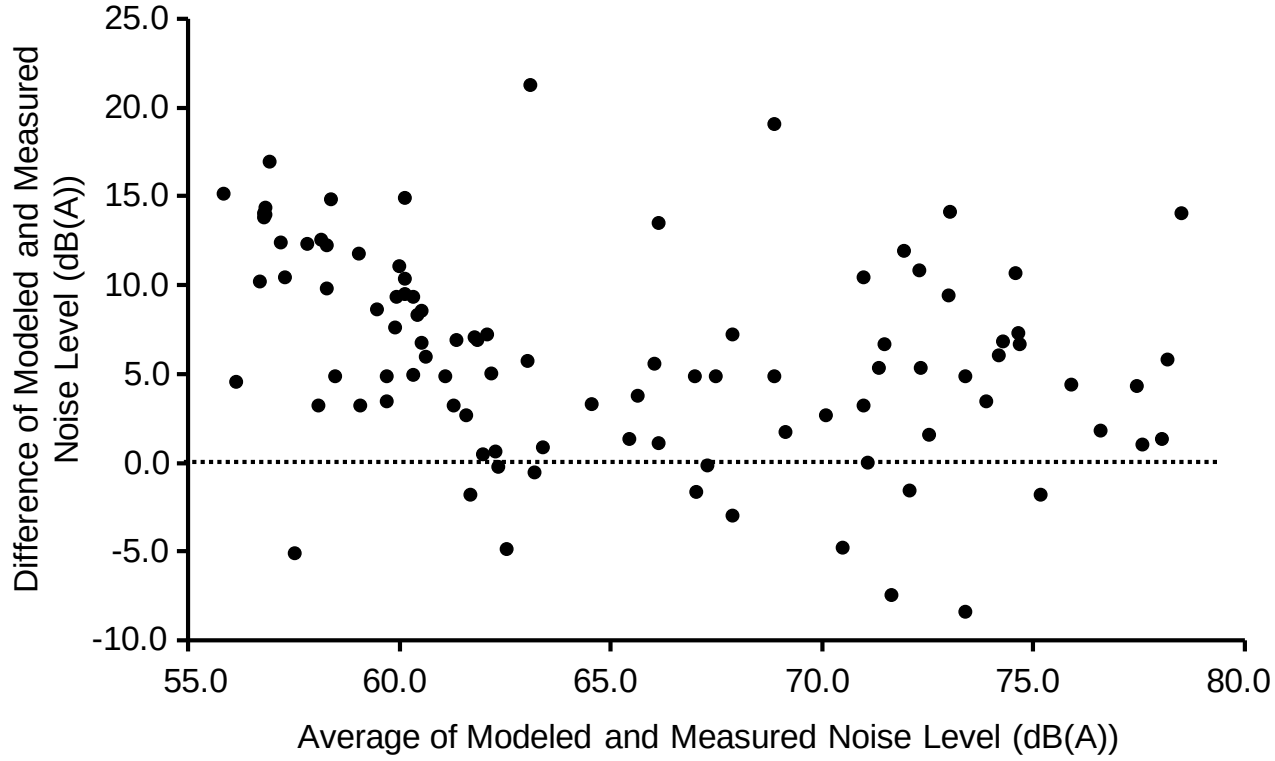
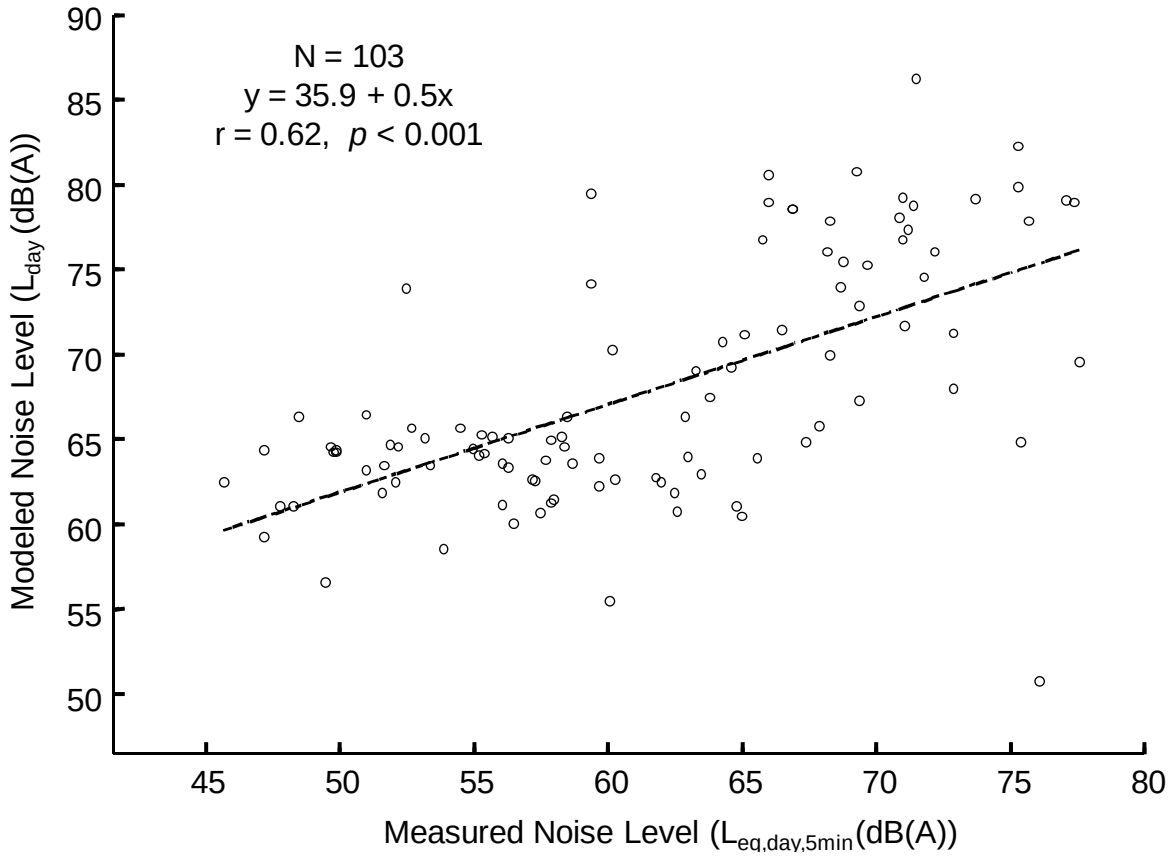


Figure 4.3 Correlations between Modeled and Measured Noise Levels



Chapter 5: Associations of Long-Term Exposure to Community Noise and Traffic-Related Air Pollution with Coronary Heart Disease Mortality

5.1 Introduction

In recent decades, convincing epidemiologic evidence has demonstrated that air pollution is associated with increased cardiovascular disease, especially coronary heart disease (CHD), morbidity and mortality.[11] Meanwhile, there is accumulating evidence that community noise including road traffic noise and aircraft noise is associated with an increased risk of CHD, especially myocardial infarction (MI).[21-23] In metropolitan areas, road traffic is a major contributor to ambient air pollution, and also the dominant source for community noise.[30, 43, 61, 62] Persons exposed to higher levels of air pollution may also be exposed to excessive traffic noise.[61, 62, 196] Therefore, a major concern in epidemiologic studies is that the observed associations between air pollution and adverse cardiovascular outcomes may be confounded by community noise and vice versa.[61, 62] Furthermore, it is possible that these coexistent environmental pollutants may interact with each other in association with an increased risk of coronary mortality.[61]

In our previous studies in metropolitan Vancouver, we found that living close to major roads was associated with a 29% (95% confidence interval (CI): 18-41%) increase in CHD mortality.[174] We further examined the associations of coronary mortality with four major traffic-related air pollutants including black carbon, particulate matter ≤ 2.5 μm in aerodynamic diameter ($PM_{2.5}$), NO_2, and NO, and found that black carbon, an indicator of traffic-related fine particulate air pollution, was associated with a 6% (95% CI, 3-9%) increase in coronary mortality; but no robust

associations were found with $PM_{2.5}$, NO_2, or NO.[162] Together, these findings suggest that exposure to the traffic-related air pollutants cannot fully explain the excess risk of coronary mortality associated with residential proximity to road traffic; traffic noise might also play a role in the observed association.

In the present study, we investigated the relationships between long-term exposure to community noise and CHD mortality as well as the independent and joint effects of community noise and traffic-related air pollution (black carbon) on the risk of CHD mortality.

5.2 Methods

5.2.1 Study Design

In British Columbia, Canada, the mandatory health insurance program managed by the Ministry of Health Services provides universal health care coverage for nearly all residents of the province.[151] We used linked administrative databases from the health insurance system to assemble this population-based cohort.[150, 162, 174] This study included a 5-year exposure period (January 1994 to December 1998) and a 4-year follow-up period (January 1999 to December 2002). All metropolitan Vancouver residents who met the following inclusion criteria at baseline (January 1999) were included in the cohort: (1) registered with the provincial health insurance plan; (2) resided in the study region during the 5-year exposure period; (3) 45 to 85 years of age; and (4) no previous diagnosis of CHD.

During the 5-year exposure period, individual exposures to community noise and traffic-related air pollutants were estimated at each person's residence (residential postal code) using a noise prediction model and land use regression (LUR) models, respectively. During the 4-year follow-up period, CHD mortality information was retrieved from the provincial death registration database. The

associations of noise and black carbon with CHD mortality were examined using the Cox proportional hazards regression model. This study was approved by the Institutional Review Board of The University of British Columbia (Behavioural Research Ethics Board certificate # H08-00185).

5.2.2 Noise Exposure Assessment

We used a noise prediction model CadnaA (Datakustik, Greifenberg, Germany) to estimate annual average community noise levels (L_{den}) at each person's residence (residential postal code) in 2003. The method has been described in detail elsewhere.[213] Briefly, noise exposure assessment was based on the following transportation-related data: road traffic data (road width, traffic volume, fleet composition, road type, speed limits, presence of traffic light, road surface, and road gradient), railway data (type of train, velocity, and frequency), building heights and footprints, and type of land use. Aircraft noise data were obtained from the aircraft noise exposure forecast contours produced by Vancouver International Airport Authority. Based on these data, annual average A-weighted equivalent continuous noise level (L_{den} dB(A)) was calculated for each area covered by a 6-digit postal code. This metric integrated noise levels during the day (6:00 am - 18:00 pm), the evening (18:00 pm - 22:00 pm), and the night (22:00 pm - 6:00 am), with a 5 dB(A) weighting added to evening noise and a 10 dB(A) weighting added to night noise to reflect increased sensitivity of residents to community noise at evening and night.[25, 27]

5.2.3 Air Pollution Exposure Assessment

We used high-resolution LUR models to estimate residential exposure to traffic-related air pollutants including black carbon, $PM_{2.5}$, NO_2, and NO in 2003 as described in detail elsewhere.[40, 154, 155] Compared with air quality monitoring data, the major advantage of LUR models is that they

are able to better describe spatial variation of intra-urban air pollution levels. Furthermore, we used air quality monitoring data to describe the long-term temporal trend of each air pollutant.[40] By combining the temporal trends with the LUR models, we calculated monthly concentrations, and then average concentrations during the 5-year exposure period for each pollutant in each postal code area.

Because the noise and air pollution exposure assessment did not cover the whole region of metropolitan Vancouver, a small proportion of study subjects with missing data were excluded from the analyses. Meanwhile, some subjects had partially missing data because of changes in residences (moving from or to areas outside the exposure assessment domain); those with missing data in more than a total of any 15 months or in more than 3 consecutive months during the 5-year exposure period were also excluded from the analyses. For those with multiple noise or air pollution levels due to changes in residences, we calculated equivalent noise levels or average air pollution levels during the exposure period. The noise data including aircraft noise data and air pollution data were assigned to study subjects through their 6-digit residential postal codes. In urban areas, a 6-digit postal code typically represents a high-rise building or one side of a city block in the study region.

5.2.4 Case Definitions

The study outcome was CHD deaths during the 4-year follow-up period. A CHD death was defined as a death record with CHD (ICD-9, 410-414 and 429.2; ICD-10, I20-I25) as the cause of death in the provincial death registration database. ICD codes for other cardiovascular diseases were presented in Table 5.1.

Subjects who were hospitalized with CHD as the principal diagnosis (the diagnosis most responsible for a hospital admission) or primary diagnosis (the diagnosis that had a substantial

influence on hospital length of stay) before baseline (based on data from January 1991 to December 1998) were regarded as previously diagnosed CHD cases and were excluded from the analysis.

5.2.5 Preexisting Comorbidity

Diabetes (ICD-9, 250; ICD-10, E10-E14),[159] chronic obstructive pulmonary disease (COPD) (ICD-9, 490-492 and 496; ICD10, J40-J44),[160, 214] and hypertensive heart disease (ICD-9, 401-404; ICD10, I10-I13)[159] are independent risk factors for CHD. In addition, these chronic diseases and CHD share common behavioral risk factors. As in our previous analyses,[162, 174] we used these preexisting comorbidities as a proxy variable for common behavioral cardiovascular risk factors.[163] To sufficiently identify subjects with preexisting comorbidities, we used all diagnoses in a hospitalization record (up to 16 diagnoses before 2001 and up to 25 diagnoses since 2001); one hospitalization record with the diagnosis of any of these chronic diseases during January 1991 to December 1998 was defined as the presence of preexisting comorbidity.

5.2.6 Neighborhood Socioeconomic Status

Because individual socioeconomic status (SES) data were not available, we used neighborhood SES to approximately estimate individual SES.[170, 171] The neighborhood-income quintiles from the 2001 Statistics Canada Census were assigned to study subjects using their residential postal codes. The method for neighborhood-income quintiles calculation has been described in detail elsewhere.[174]

5.2.7 Statistical Analysis

The baseline characteristics between study subjects across deciles of noise levels were compared using a chi-square test for categorical variables, one-way analysis of variance for continuous variables, and Tukey's post hoc analysis for pair-wise comparisons of continuous variables. Correlations between pollutants were examined using Spearman's rank correlation analysis.

The Cox proportional hazards regression model was used to determine the associations between noise or air pollution and CHD mortality; age, sex, preexisting comorbidity, neighborhood SES were included as covariates; air pollutants or noise were added in the final models. Person-years of observation were calculated from baseline to the date of CHD death or end of follow-up. For those who died from other diseases or moved out of the province, person-years were calculated from baseline to the date of death or the last known date in the province.

We first treated noise levels as a continuous variable to calculate relative risks (RRs) for CHD mortality associated with a 10 dB(A) elevation in noise levels. We then treated noise levels as a categorical variable to examine exposure-response relationships by dividing study subjects into deciles based on the noise levels; RRs of coronary mortality were calculated for each decile by using decile 1 (lowest) as the reference category. The results were presented by four groups of study subjects: decile 1, deciles 2-5, deciles 6-9, and decile 10.

All statistical analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, NC, USA). All statistical tests were 2-sided.

5.3 Results

A total of 466,727 subjects who met the inclusion criteria were included at baseline. Among these subjects, 13,992 (3.0%) with missing air pollution data were excluded; an additional 6,867 (1.5%) with missing noise data were further excluded, which left 445,868 subjects for the present analysis. After the 4-year follow-up period, there were 412,420 subjects in the cohort with complete information; the overall follow-up rate was 92.5%.

For this cohort, the annual average noise level was 63.4 (interquartile range (IQR), 59.8 - 66.4) dB(A) (Table 5.2). Overall, noise levels were not strongly correlated with traffic-related air pollutant concentrations, the highest correlation was with black carbon (r = 0.44), the lowest correlation was with $PM_{2.5}$ (r = 0.14). Traffic-related air pollutants were weakly correlated with each other, with the exception of NO_2 and NO (Table 5.2).

Table 5.3 shows the characteristics of study subjects at baseline by deciles of noise levels. Compared with those exposed to lower noise levels (decile 1), subjects exposed to higher noise levels were more likely to have preexisting comorbidity and lower neighborhood SES (Table 5.3).

During the 4-year follow-up period, 3,095 subjects died of CHD, and the mortality rate was 1.83 per 1000 person-years. Residential noise exposure was strongly associated with CHD mortality; a 10 dB(A) elevation in noise levels was associated with a 26% (95% CI, 17-35%) increase in CHD mortality. Adjusting for age, sex, preexisting comorbidity, and neighborhood SES halved the estimated relative risk, while further adjustment for $PM_{2.5}$ and NO_2 had little influence on effect estimates. Additionally adjusting for back carbon had a greater influence on the effect estimate, but a 10 dB(A) elevation in noise levels was still associated with a 9% (95% CI, 1-18%) increase in CHD mortality (Table 5.4). For other cardiovascular diseases such as stroke, dysrhythmias, and congestive

heart failure, there was no significant increase in mortality associated with a 10 dB(A) elevation in noise levels (Table 5.5).

When study subjects were categorized into decile groups based on noise levels, compared with those in decile 1 with noise levels ≤ 58 dB(A), subjects in deciles 2-5 and deciles 6-9 had little increase in coronary mortality, while those in decile 10 exposed to noise levels >70 dB(A) had a 22% (95% CI, 4-43%) increase in coronary mortality after adjusting for all covariates including traffic-related air pollutants, suggesting that there was no linear exposure-response relationship between noise and coronary mortality (P = 0.174 for test of linear trend across decile groups in the fully adjusted model) (Table 5.4).

Figure 5.1 shows that both noise and black carbon exposure were independently associated with coronary mortality, an IQR elevation in noise (6.6 dB(A)) and black carbon (0.97×10^{-5}/m) was associated with a 6% (95% CI, 1-11%) and a 4% (95% CI, 1-8%) increase in coronary mortality, respectively. We did not find any positive interaction between noise and black carbon on coronary mortality when assessed on either additive (Table 5.6) or multiplicative (P = 0.980 for the interaction term in the fully adjusted model) scales.

Stratified analysis shows that in the fully adjusted model coronary mortality associated with a 10 dB(A) elevation in noise levels was greater for females, those aged ≥ 65 years, with preexisting comorbidity, and with higher neighborhood SES. However, there was considerable overlap in the 95% CIs between these subgroups (Table 5.7).

For those exposed to aircraft noise (N = 294,783), annual average noise level was 32 (IQR, 22-45) dB(A). Compared with road traffic noise, aircraft noise was less correlated (r = -0.10 to 0.33) with traffic-related air pollution (Table 5.8). There was no significant increase in coronary mortality associated with exposure to aircraft noise (Table 5.9).

5.4 Discussion

This large population-based cohort study found that a 10 dB(A) elevation in residential noise levels (L_{den}) was associated with a 9% increase in CHD mortality, after adjustment for the various covariates including traffic related air pollutants. There was no discernable linear exposure-response relationship; persons in the highest decile of noise levels (>70 dB(A)) had a 22% increase in coronary mortality compared with those in the lowest decile (≤ 58 dB(A)). Also in the fully adjusted model, an IQR (0.97×10^{-5}/m) elevation in black carbon concentrations was associated with a 4% increase in CHD mortality. We did not find any positive interaction between noise and black carbon on coronary mortality. For those exposed to aircraft noise, there was no significant increase in coronary mortality compared with the non-exposed persons.

The findings from previous studies on community noise and cardiovascular disease are not consistent and the reported associations have been only borderline significant, but most previous studies show positive associations between exposure to community noise and coronary events. In a 9-year Dutch cohort study with 117,528 participants,[89] Beleen et al examined the effects of exposure to both road traffic noise and black smoke on cardiovascular disease mortality. Cardiovascular mortality increased 17% (95% CI, -6 to 45%) for those exposed to higher levels of traffic noise (> 65 vs. ≤ 50 dB(A)), and 11% in response to a 10 $\mu g/m^3$ increase in black smoke concentrations; however, there was no discernible increase in coronary mortality.[89] In a population-based case-control study in Stockholm County,[22] Selander et al found that long term exposure to higher levels of road traffic noise (≥50 vs. <50 dB(A)) was associated with a 12% (95% CI, -5 to 33%) increase in the risk of MI after adjusting for the indictor of traffic-related air pollution (NO_2) and other cardiovascular risk factors. After further excluding those with hearing loss or with other sources of noise exposure, the risk of MI increased by 38% (95% CI, 11-71%).[22] In a 5-year Swiss National

Cohort Study with 4.6 million subjects,[23] Huss et al found that people exposed to higher levels of aircraft noise (≥ 60 vs. < 45 dB(A)) had a 30% (95% CI, -4 to 76%) increase in MI mortality after adjusting for particulate air pollution (PM_{10}), residential proximity to major roads, and other covariates; when the analysis was restricted to those who lived in their residences for at least 15 years, the MI mortality increased by 48% (95% CI, 1-118%).[23] Some previous studies on the association of noise exposure with CHD risk did not adjust for coexistent traffic-related air pollution. In a case-control study with 1881 MI patients and 2234 controls in Berlin,[21] Babisch et al found that men exposed to higher levels of road traffic noise (>70 vs. ≤ 60 dB(A)) had an odds ratio (OR) of 1.27 (95% CI, 0.88 to 1.84) for MI; for those who lived at their residences for at least 10 years, the OR was 1.81 (95% CI, 1.02 to 3.21); but the association was not observed among women.[21] In a 10-year cohort study with 4,860 males,[90] Babisch et al observed a non-significant increase in coronary events for those exposed to higher levels of road traffic noise (≥ 66 vs. ≤ 55 dB(A)).[90] In these previous studies and also in the present study, there was not an ideal control group without community noise exposure; therefore, low-level exposure group was used as the reference category. Small noise exposure contrasts might limit the statistical power to detect relatively small adverse cardiovascular effects. In addition, as discussed previously,[162] several previous studies have also shown that exposure to black carbon was associated with increased coronary mortality. However, most of these previous studies did not take into account coexistent community noise.[162]

Potential biological mechanisms for these epidemiologic associations have been proposed, but the precise mechanisms linking community noise exposure with cardiovascular mortality have not been fully elucidated. Psychosocial stress has been demonstrated to be an independent risk factor for cardiovascular disease.[130-132] Chronic exposure to noise may cause sleep disturbance, annoyance, speech interference, and psychosocial stress;[25, 27, 148] therefore, chronic noise exposure may serve as a

potent environmental stressor to activate sympathetic nervous and endocrine system to release stress hormones such as noradrenaline and cortisol.[137, 215, 216] Stress hormones bind with beta-adrenergic receptors in the heart and blood vessels,[139] leading to increased myocardial contractility, flow velocity, coronary artery constriction, vulnerable plaque rupture and thrombosis, and subsequent myocardial ischemia or infarction.[139, 217-219] As discussed previously,[162] there is also convincing pathophysiological evidence such as pulmonary and systemic oxidative stress and inflammation to support the associations between exposure to black carbon and coronary mortality.[11]

This study shows that the correlations between modeled community noise and air pollution levels range from 0.14 ($PM_{2.5}$) to 0.44 (black carbon), which is within the range of correlations reported in previous studies.[61, 62, 196] In practice, some road traffic factors such as speed, volume, and operating conditions may differentially affect the emission levels of traffic noise and traffic-related air pollution.[88, 208, 209] For example, when vehicle speed is less than 30 km/h during traffic congestion, noise levels are lower; but air pollution emissions are relatively higher. However, when vehicle speed is over 40 km/h, noise levels, mainly from tire-road interaction, are rapidly increased; but air pollution emissions are relatively lower.[88, 209] Furthermore, traffic-related air pollution is strongly dependent on traffic volume; but traffic volume has smaller influence on traffic noise. For example, when traffic volume is doubled, traffic noise levels increase only 3 dB(A).[88] In addition, some environmental factors such as road pavement materials, noise barriers, and surrounding buildings have little influence on air pollution levels; but these factors may strongly affect road traffic noise levels, especially when vehicle speed is over 40 km/h.[88] Finally, meteorological factors such as wind direction and speed may strongly affect traffic-related air pollution, but have smaller influence on traffic noise levels.[62] Rain and wet road surface may substantially increase road traffic

noise, but may substantially decrease ambient air pollution. All these factors may partly explain the low-to-moderate correlations between noise and traffic-related air pollution in the study region.

Previous findings on sex differences in the association between noise exposure and coronary mortality are not consistent. Some studies found men are more susceptible to noise exposure than women,[21] whereas other studies found no differences between men and women.[22, 89] Our study shows that men and women had similar risk of coronary mortality associated with a 10 dB(A) elevation in noise levels; however after adjusting for traffic-related air pollutants including $PM_{2.5}$, NO_2 and black carbon, women had a 7% excess risk of coronary mortality compared with men, although the difference was not statistically significant. This observation is consistent with the findings of Willich et al[220] and is supported by the findings that women had greater levels of salivary cortisol than did men in response to noise exposure.[216, 221]

This study had some limitations that should be considered. First, the exposure assessment was based on the residential postal codes of study subjects to estimate the exposure at their residences. This method cannot precisely reflect actual individual exposure,[52, 190] because many environmental factors such as street canyons,[172] wind direction,[62] roadside noise barriers, and specific housing characteristics [51]as well as individual factors such as noise sensitivity,[222] the time spent at home,[52, 222] living room/bedroom orientation,[222] and occupational noise exposure[92, 98] might substantially affect actual individual exposure. Nevertheless, these factors are likely to cause non-differential exposure misclassification, leading to underestimations of true risk of coronary mortality associated with exposure to noise and traffic-related air pollution.[190]

Second, because the cohort was constructed using linked administrative databases from the provincial health insurance system, some individual-level cardiovascular risk factors were not available and thus could not be controlled in the data analysis. We adjusted for preexisting

comorbidity including diabetes, COPD, and hypertensive heart disease. Because these comorbidities and CHD share common behavioral risk factors, adjusting for these comorbidities to some extent was able to reduce the influence of unmeasured risk factors and these comorbidities themselves on the effect estimates.[163] In addition, as discussed previously,[162, 174] although cigarette smoking is the single most important risk factor for coronary mortality,[164] it does not substantially affect the associations between fine particulate air pollution and CHD.[70, 83] Similarly, recent studies have also shown that cigarette smoking (either smoking status or daily smoking amount) does not substantially affect the associations between noise exposure and coronary events.[22, 89]

Third, low individual SES is a risk factor for CHD [165] and those with low SES are more likely to be exposed to community noise and traffic-related air pollution.[169] Individual SES is thus a possible confounder for the observed associations. As discussed before,[162, 174] individual SES was not available in this study, we used neighborhood income quintiles to approximate individual SES. There is some evidence that this approach is valid for control of individual SES.[170, 171] In addition, in a subgroup analysis of the study subjects (n = 1194) who participated in the Canadian Community Health Survey (2000-2001), neighborhood income quintiles were strongly associated with individual annual household income, education level, marital status, and daily fruit and vegetable intake (all $P < 0.001$) (Table 5.10). Based on these results, we believe that including neighborhood income quintiles in the Cox model could effectively minimize the confounding effects of individual SES.

Finally, A-weighted equivalent sound pressure level based on the equal energy principle over a specific time period has been widely used in community noise exposure assessment.[21-23, 25, 89, 90] This method may be appropriate for continuous noise such as road traffic noise, but it cannot reflect actual disturbance caused by aircraft noise (e.g. average 32 dB(A) for the present study), which is

composed of a small number of high-level discrete noise events.[25] This problem may partly explain the null association between aircraft noise and coronary mortality in our study.

In conclusion, in this large population-based cohort study, we found that a 10 dB(A) elevation in residential noise levels (L_{den}) was associated with a 9% increase in CHD mortality. There was no discernable linear exposure-response relationship; subjects in the highest noise decile (>70 dB(A)) had a 22% increase in CHD mortality compared with those in the lowest decile (≤ 58 dB(A)). An IQR (0.97×10^{-5}/m) elevation in black carbon concentrations was associated with a 4% increase in CHD mortality. We did not find any positive interaction between noise and black carbon on coronary mortality. These findings suggest that both community noise and traffic-related fine particulate air pollution indicated by black carbon may be partly responsible for the observed associations between exposure to road traffic and adverse cardiovascular outcomes.

Table 5.1 ICD Codes and Number of Deaths During the Follow-Up Period

Cause of Death[a]	ICD-9 Codes	ICD-10 Codes	No. of Deaths
All cardiovascular diseases	390-459	I00-I99	4171
Coronary heart disease[b]	410-414, 429.2	I20-I25	3095
Acute myocardial infarction	410	I21, I22	1754
Acute coronary heart disease	410, 411	I21, I22, I24	1790
Chronic coronary heart disease	412-414, 429.2	I20, I25	1305
Hypertensive heart disease	402, 404	I11, I13	122
Cardiac dysrhythmias	427	I46-I49	221
Congestive heart failure	428	I50	277
Stroke[b]	430-434, 436-438	I60-I69	1288
Ischemic stroke	433, 434, 436	I63, I65, I66, I67.2, I67.8	257
Hemorrhagic stroke	430-432	I60-I62	337
All other cardiovascular diseases	390–459, excluding those specified	I00-I99, excluding those specified	902

[a] For each disease, the prior cases for the disease were excluded, unless otherwise specified.

[b] For the subcategories of the disease, all prior cases of the disease were excluded.

Table 5.2 Average Noise Levels, Traffic-Related Air Pollutant Concentrations, and Correlations

Pollutant	Mean (SD)	Median	IQR	Range	Correlation Coefficient[a]				
					Noise	BC	$PM_{2.5}$	NO_2	NO
Noise (L_{den} dB(A))	63.4 (5.0)	62.4	59.8-66.4	33.0-90.0	1.00	--	--	--	--
BC (10^{-5}/m)	1.50 (1.10)[b]	1.02	0.83-1.80	0.0-4.98	0.44	1.00	--	--	--
$PM_{2.5}$ ($\mu g/m^3$)	4.10 (1.64)	4.04	3.22-4.81	0.0-10.24	0.14	0.13	1.00	--	--
NO_2 ($\mu g/m^3$)	32.3 (8.1)	30.8	26.7-35.2	15.3-57.5	0.33	0.39	0.47	1.00	--
NO ($\mu g/m^3$)	32.2 (12.0)	29.5	24.3-37.6	8.8-126.0	0.39	0.43	0.43	0.66	1.00

Abbreviations: BC, black carbon; IQR, interquartile range; L_{den} dB(A), annual day-evening-night A-weighted equivalent continuous noise level.SD, standard deviation.

[a] $P < 0.001$ for each correlation coefficient.

[b] 1.20 (0.88) $\mu g/m^3$ elemental carbon (10^{-5}/m black carbon $\approx$ 0.8 $\mu g/m^3$ elemental carbon).

Table 5.3 Baseline Characteristics of Study Subjects by Deciles of Noise Levels

Covariate [a,b]	Deciles of Noise Levels (L_{den} dB(A))			
	Decile 1 (≤ 58)	**Deciles 2-5 (59 - 62)**	**Deciles 6-9 (63 - 70)**	**Decile 10 (> 70)**
Men (%)	46.0	46.6	45.9	45.8
Age (SD) (years)	59.3 (10.8)	59.0 (10.6)	59.4 (10.7)	60.0 (10.9)
Comorbidity (%)				
Diabetes	2.1	2.1	2.4	2.9
COPD	1.5	1.3	1.5	1.8
Hypertensive heart disease	4.3	4.0	4.3	4.8
Any of the above	6.6	6.3	6.8	7.9
Income quintile (%)[c]				
1	11.8	14.8	21.4	28.3
2	13.4	18.5	20.0	23.2
3	17.3	20.3	19.4	17.4
4	25.3	21.9	18.7	15.3
5	32.3	24.5	20.4	15.9

Abbreviations: COPD, chronic obstructive pulmonary disease; L_{den} dB(A), annual day-evening-night A-weighted equivalent continuous noise level.

[a] $P \leq 0.001$ for all comparisons between groups.

[b] Percentage for categorical variable, mean (SD) for continuous variable.

[c] Quintile 1 represents the lowest, quintile 5 the highest neighborhood income quintile.

Table 5.4 RRs and 95% CIs for Coronary Heart Disease Mortality Associated with a 10 dB(A) Elevation in Noise Levels or by Deciles of Noise Levels

Model	10 dB(A) Elevation		Deciles of Noise Levels (L_{den} dB(A))						
			Decile 1 (≤ 58)	Deciles 2-5 (59-62)		Deciles 6-9 (63-70)		Decile 10 (> 70)	
	RR	95% CI	Reference	RR	95% CI	RR	95% CI	RR	95% CI
(1) Unadjusted	1.26	1.17, 1.35	1.00	1.01	0.89, 1.15	1.09	0.96, 1.24	1.49	1.28, 1.73
(2) Model (1) + sex, age	1.18	1.10, 1.26	1.00	1.06	0.93, 1.20	1.09	0.96, 1.24	1.39	1.20, 1.61
(3) Model (2) + comorbidity, SES	1.13	1.06, 1.21	1.00	1.05	0.92, 1.19	1.06	0.93, 1.20	1.30	1.12, 1.51
(4) Model (3) + $PM_{2.5}$	1.13	1.06, 1.21	1.00	1.04	0.91, 1.19	1.05	0.92, 1.20	1.29	1.11, 1.50
(5) Model (4) + NO_2	1.12	1.05, 1.21	1.00	1.05	0.92, 1.20	1.05	0.92, 1.20	1.28	1.10, 1.50
(6) Model (5) + black carbon	1.09	1.01, 1.18	1.00	1.04	0.91, 1.19	1.02	0.89, 1.17	1.22	1.04, 1.43

Abbreviations: CI, confidence interval; L_{den} dB(A), annual day-evening-night A-weighted equivalent continuous noise level; RR, relative risk; SES, neighborhood socioeconomic status.

Table 5.5 RRs and 95% CIs for Cardiovascular Disease Mortality Associated with a 10 dB(A) Elevation in Noise Levels

Cause of Death	Model 1[a]		Model 2[b]		Model 3[c]	
	RR	95% CI	RR	95% CI	RR	95% CI
All cardiovascular diseases	1.22	1.15, 1.30	1.11	1.05, 1.18	1.07	1.00, 1.15
Coronary heart disease	1.26	1.17, 1.35	1.13	1.06, 1.21	1.09	1.01, 1.18
Acute myocardial infarction	1.25	1.14, 1.36	1.13	1.03, 1.24	1.08	0.97, 1.19
Acute coronary heart disease	1.26	1.15, 1.37	1.14	1.04, 1.25	1.09	0.98, 1.20
Chronic coronary heart disease	1.26	1.13, 1.40	1.13	1.01, 1.25	1.09	0.97, 1.23
Hypertensive heart disease[d]	1.18	0.84, 1.67	1.08	0.76, 1.53	1.18	0.80, 1.75
Cardiac dysrhythmias	1.20	0.93, 1.56	1.13	0.87, 1.46	1.08	0.81, 1.43
Congestive heart failure	1.32	1.05, 1.65	1.19	0.95, 1.49	1.15	0.89, 1.48
Stroke	1.16	1.05, 1.30	1.06	0.96, 1.18	1.03	0.91, 1.16
Ischemic stroke	1.15	0.90, 1.46	1.01	0.80, 1.28	1.02	0.78, 1.33
Hemorrhagic stroke	1.26	1.03, 1.55	1.17	0.95, 1.44	1.14	0.91, 1.44
All other cardiovascular diseases	1.19	1.05, 1.36	1.10	0.97, 1.25	1.02	0.89, 1.18

[a] Model 1: bivariable analysis.

[b] Model 2: adjusted for age, sex, preexisting comorbidity, and neighborhood SES.

[c] Model 3: further adjusted for traffic-related air pollutants including $PM_{2.5}$, NO_2, and black carbon.

[d] Preexisting comorbidity was replaced by two variables COPD (yes, no) and diabetes (yes, no).

Table 5.6 RRs and 95% CIs for Coronary Heart Disease Mortality by Deciles of Noise Levels and Quartiles of Black Carbon Concentrations

Quartiles of Black Carbon	Deciles of Noise Levels (L_{den} dB(A))							
	Decile 1 (≤ 58)		Deciles 2-5 (59-62)		Deciles 6-9 (63-70)		Decile 10 (> 70)	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Quartile 1 ($0 - 0.83 \times 10^{-5}$/m)	1.00	Reference	1.11	0.88, 1.40	1.12	0.86, 1.45	1.29	0.79, 2.12
Quartile 2 ($0.84 - 1.02 \times 10^{-5}$/m)	1.05	0.78, 1.41	1.09	0.87, 1.37	1.06	0.84, 1.34	1.24	0.88, 1.74
Quartile 3 ($1.03 - 1.80 \times 10^{-5}$/m)	1.09	0.79, 1.49	1.23	0.97, 1.55	1.18	0.94, 1.49	1.48	1.09, 2.02
Quartile 4 ($1.81 - 4.98 \times 10^{-5}$/m)	1.50	1.04, 2.17	1.21	0.93, 1.56	1.23	0.98, 1.54	1.45	1.14, 1.85

Abbreviation: L_{den} dB(A), annual day-evening-night A-weighted equivalent continuous noise level.

Adjusted for age, sex, preexisting comorbidity, neighborhood income quintiles, and co-pollutants (NO_2 and $PM_{2.5}$).

Table 5.7 RRs and 95% CIs for Coronary Heart Disease Mortality Associated with a 10 dB(A) Elevation in Noise Levels, Stratified by Each Covariate

Subgroup	Percentage (%)	Model 1		Model 2		Model 3	
		RR	95% CI	RR	95% CI	RR	95% CI
Sex							
Male	46.2	1.28	1.17, 1.39	1.15	1.05, 1.26	1.07	0.97, 1.18
Female	53.8	1.24	1.11, 1.39	1.11	0.99, 1.23	1.12	0.99, 1.27
Age, years							
< 65 years	68.0	1.21	1.03, 1.43	1.07	0.91, 1.27	1.03	0.85, 1.25
≥ 65 years	32.0	1.18	1.10, 1.28	1.14	1.06, 1.23	1.09	1.00, 1.19
Comorbidity							
No	93.3	1.22	1.13, 1.33	1.11	1.02, 1.20	1.07	0.98, 1.18
Yes	6.7	1.20	1.06, 1.35	1.18	1.05, 1.33	1.10	0.96, 1.26
Income quintiles							
High (4-5)	43.1	1.32	1.17, 1.49	1.19	1.05, 1.34	1.12	0.97, 1.29
Low (1-3)	56.9	1.14	1.05, 1.24	1.12	1.03, 1.22	1.06	0.97, 1.17

Model 1: bivariable analysis; Model 2: adjusted for age, sex, preexisting comorbidity, and neighborhood SES; Model 3: further adjusted for traffic-related air pollutants including $PM_{2.5}$, NO_2, and black carbon.

Table 5.8 Average Aircraft Noise Levels, Traffic-Related Air Pollutant Concentrations, and Correlations

Pollutant	Mean (SD)	Median	IQR	Range	Correlation Coefficient[a]				
					Noise	BC	$PM_{2.5}$	NO_2	NO
Noise (L_{den} dB(A))	32.0 (16.5)	35.3	21.6-44.5	0.0-71.0	1.00	--	--	--	--
BC (10^{-5}/m)	1.56 (1.14)[b]	1.05	0.83-1.95	0.0-4.98	-0.10	1.00	--	--	--
$PM_{2.5}$ ($\mu g/m^3$)	4.30 (1.55)	4.21	3.49-4.97	0.0-10.23	0.33	0.07	1.00	--	--
NO_2 ($\mu g/m^3$)	34.1 (7.4)	32.5	29.5-36.2	17.8-57.5	0.19	0.37	0.41	1.00	--
NO ($\mu g/m^3$)	35.3 (12.5)	33.1	26.7-40.2	10.9-126.0	0.33	0.44	0.42	0.62	1.00

Abbreviations: BC, black carbon; IQR, interquartile range; L_{den} dB(A), annual day-evening-night A-weighted equivalent continuous noise level.

[a] N = 294,783, $P < 0.001$ for each correlation coefficient.

[b] 1.25 (0.91) $\mu g/m^3$ elemental carbon (10^{-5}/m black carbon $\approx$ 0.8 $\mu g/m^3$ elemental carbon).

Table 5.9 RRs and 95% CIs for Coronary Heart Disease Mortality by Quartiles of Aircraft Noise Levels

Model[a]	Quartiles of Aircraft Noise Levels (L_{den} dB(A))							
	Quartile 1		Quartile 2		Quartile 3		Quartile 4	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Unadjusted	1.17	1.05,1.29	1.21	1.09, 1.34	1.04	0.93, 1.16	0.96	0.86, 1.08
Adjusted for age, sex, SES, comorbidity	1.20	1.09, 1.34	1.15	1.04, 1.27	1.01	0.91, 1.13	0.94	0.85, 1.06
Further adjusted for BC, $PM_{2.5}$, and NO_2	1.19	1.07, 1.33	1.11	0.99, 1.24	1.00	0.88, 1.13	0.93	0.82, 1.05

Abbreviations: BC, black carbon; L_{den} dB(A), annual day-evening-night A-weighted equivalent continuous noise level; SES, neighborhood socioeconomic status.

[a] N = 445,868, non-exposed subjects were used as the reference category. Quartile 1 represents the lowest noise group; Quartile 4, the highest noise group.

Table 5.10 Associations between Neighborhood Income Quintiles and Cardiovascular Risk Factors

Risk Factors[a]	Neighborhood Income Quintiles (1 = Lowest, 5 = Highest)					
	Quintle 1 (n = 217)	Quintle 2 (n = 220)	Quintle 3 (n = 265)	Quintle 4 (n = 278)	Quintle 5 (n = 214)	*P* Value[b]
Male (%)	43.3	40.9	37.7	48.2	43.0	0.169
Age (year)	65.2 (12.2)	63.3 (11.3)	61.3 (11.0)	61.3 (11.2)	61.1 (11.2)	< 0.001
Race, white (%)	80.6	82.7	86.4	85.3	89.3	0.105
Body mass index (kg/m^2)	25.5 (4.7)	25.2 (4.4)	25.8 (4.5)	25.6 (4.4)	24.3 (3.5)	0.002
Education ≤ secondary school (%)	59.0	56.8	41.5	33.5	33.6	< 0.001
Marital status (%)						< 0.001
Married	38.3	51.8	61.1	61.9	72.3	--
Separated	47.5	39.1	29.4	29.1	20.2	--
Never married	14.3	9.1	9.4	9.0	7.5	--
Cigarette smoking (%)						0.052
Current smoker	42.4	42.7	41.1	44.2	47.7	--
Former smoker	38.7	41.4	47.6	45.7	42.5	--
Never smoker	18.9	15.9	11.3	10.1	9.8	--
Passive smoking (%)	18.5	15.1	16.6	12.6	11.8	0.315
Alcohol drinking in past 12 months (%)	66.4	71.8	76.5	76.3	80.8	0.007
Daily fruit and vegetable intake < 5 times/servings (%)	62.2	62.2	50.6	54.4	41.1	< 0.001
Physical activity (%)						0.056
Active	29.2	21.0	23.3	25.8	31.4	--
Moderate	23.9	25.2	31.2	31.1	29.5	--
Inactive	46.9	53.8	45.5	43.1	39.1	--
Unemployment last week (%)[c]	56.9	48.6	41.9	43.6	45.0	0.038
Annual household income (×1000$)[d]	24.5 (14.0-45.0)	40.0 (22.0-60.0)	47.0 (28.5-80.0)	47.0 (26.0-75.0)	75.0 (40.0-100.0)	< 0.001

[a] For subjects who participated in the Canadian Community Health Survey (2000-2001) (N = 1194). The number is slightly different for each variable, unless otherwise specified. Percentage for categorical variable, mean (SD) for continuous variable.

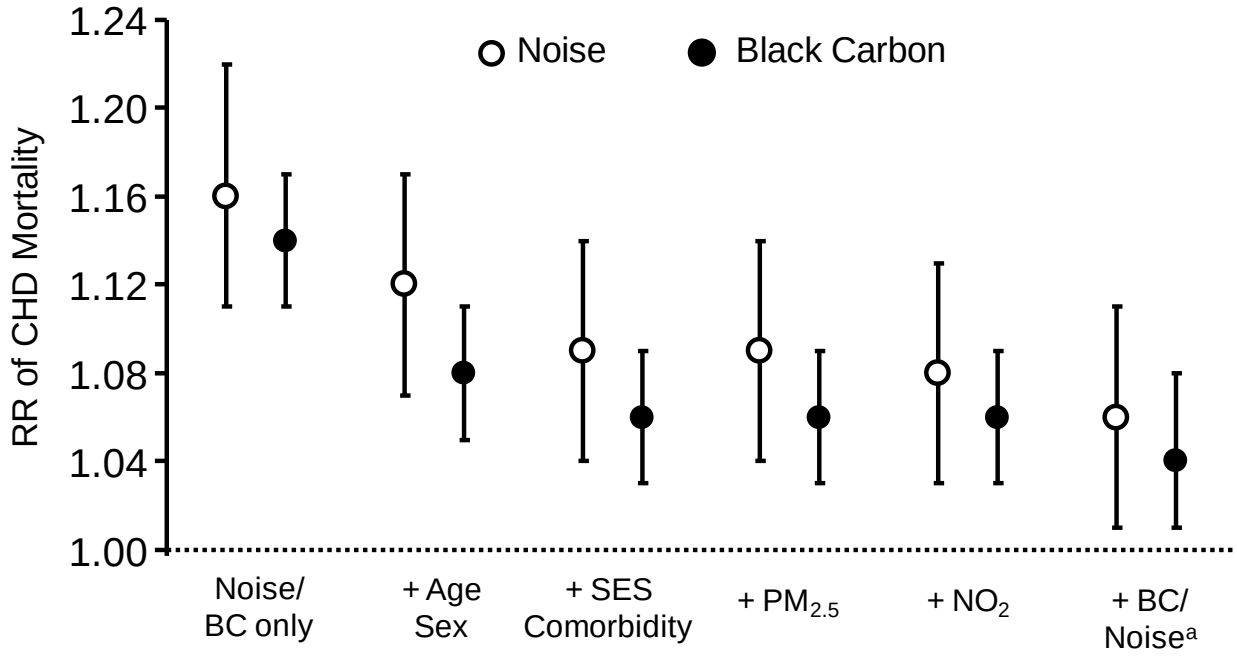
[b] Overall comparison between five groups: χ^2 test for categorical variables, and one-way analysis of variance for continuous variables, unless otherwise specified.

[c] For participants applicable to this question, n = 989 (160, 177, 222, 241, 189 for each column).

[d] Median (interquartile range); *P* value is from Kruskal-Wallis Test.

Figure 5.1 RRs and 95% CIs for Coronary Heart Disease Mortality Associated with an IQR Elevation in Noise Levels or Black Carbon Concentrations

[a] Further adjusted for black carbon for noise, adjusted for noise for black carbon.



Chapter 6: Conclusions

6.1 Summary of Findings

This dissertation describes a series of analyses to assess associations of coronary heart disease (CHD) morbidity and mortality with residential proximity to road traffic, traffic-related air pollution, and community noise in metropolitan Vancouver, Canada. Linked administrative databases from the provincial health insurance system were used to assemble this cohort, which comprised all residents aged 45-85 years who resided in the study region for at least 5 years at baseline. During a 4-year follow-up period, CHD hospitalizations and deaths were identified from provincial hospitalization records and death registration records, respectively.

In the first analysis, the distances from each person's residence to major roads were used to represent different exposures to traffic-related pollution.[174] Compared with people consistently living away from major roads (e.g. > 50 m), those consistently living close to major roads (e.g. $\leq$ 50 m) had a 29% (95% CI, 18-41%) increase in the risk of coronary mortality; for those who moved closer to road traffic, the risk increased by 20% (95% CI, 0-43%); and for those who moved away from road traffic, the risk increased by 14% (95% CI, -5 to 37%).[174] Living close to road traffic signified exposures to traffic-related air pollution and traffic noise, both of which could be responsible for the observed associations between traffic proximity and coronary mortality.

The associations were further explored with land use regression models to estimate residential exposures to the major traffic-related air pollutants including black carbon, $PM_{2.5}$, NO_2, and NO.[162] An interquartile range (IQR) elevation in black carbon concentration was associated with a 3% (95% CI, 1-5%) increase in CHD hospitalization and a 6% (95% CI, 3-

9%) increase in CHD mortality. There was a clear exposure-response relationship for the observed association; but no robust associations were found with $PM_{2.5}$, NO_2, or NO.[162] These findings suggest that exposure to traffic-related fine particulate air pollution, indicated by black carbon, may partly explain the associations between exposure to road traffic and adverse cardiovascular outcomes.

A noise prediction model was then used to estimate annual average community noise levels from transportation sources for each postal code area in the study region.[213] On average, the modeled noise level was 64 (IQR, 60-68) dB(A). Overall, modeled noise levels were not strongly correlated with land use regression estimates of traffic-related air pollutants, suggesting that it was feasible to take into account both traffic-related air pollution and community noise in epidemiologic studies of traffic-related pollution and adverse cardiovascular outcomes.[213]

Finally, after adjusting for various covariates including community noise and traffic-related air pollutants, a 10 dB(A) elevation in community noise levels was associated with a 9% (95% CI, 1-18%) increase in CHD mortality. There was no linear exposure-response relationship; persons in the highest noise decile (>70 dB(A)) had a 22% (95% CI, 4-43%) increase in CHD mortality compared with those in the lowest decile (≤ 58 dB(A)). An IQR elevation in community noise (6.6 dB(A)) and black carbon (0.97×10^{-5}/m) was associated with a 6% (95% CI, 1-11%) and a 4% (95% CI, 1-8%) increase in coronary mortality, respectively. There were no discernible interactions between community noise and black carbon on coronary mortality.[223] These findings suggest independent effects of traffic-related noise and air pollution on CHD mortality.

6.2 Strengths

There are several important strengths to these analyses. First, this large population-based cohort included all residents in metropolitan Vancouver who met the inclusion criteria at baseline. The large sample size and statistical power enabled these analyses to detect the adverse cardiovascular effects with relatively higher precision.

Second, detailed residential history information was included, which provided a unique opportunity to examine the effects of changes in traffic proximity on the risk of coronary mortality like a natural experiment. The analyses found that living close to major roads was associated with CHD mortality and changes in the distances were associated with altered mortality risk in an exposure-response fashion. Furthermore, the exposure assessment for traffic-related air pollution and community noise took into account changes in residences. This method could effectively reduce exposure misclassification from residence relocation.

Third, land use regression (LUR) models can better describe spatial variability of air pollution levels, and air quality monitoring data can better describe long-term temporal variability of air pollution levels. These analyses integrated both spatial and long-term temporal variability of traffic-related air pollution in the exposure assessment. This approach could improve the accuracy of air pollution exposure assessment and increase exposure contrasts.

Finally, a noise prediction model was used to estimate annual average noise levels at each 10×10 m grid in the study region, noise levels for each postal code area were calculated based on the noise levels at these grids. The use of higher-resolution grids could effectively reduce measurement error. In data analyses, noise levels were treated as both

continuous and categorical variables, and the findings were consistent even after adjusting for traffic-related air pollutants including black smoke, $PM_{2.5}$, and NO_2.

6.3 Limitations

Despite these strengths, a number of limitations were inherent in these analyses. As this study cohort was assembled using linked administrative databases from the provincial health insurance system, some individual cardiovascular risk factors such as cigarette smoking and individual socioeconomic status (SES) were not available and thus could not be directly controlled in data analysis. To reduce the potential confounding effects of cigarette smoking and other behavioral risk factors, preexisting comorbidity including diabetes, COPD, and hypertensive heart disease was used as a proxy variable of common behavioral risk factors.[163] Because CHD and these chronic diseases share common behavioral risk factors, adjusting for these comorbidities was able to partially reduce the influence of unmeasured behavioral risk factors on the effect estimates.[163] In addition, based on literature reviews of previous epidemiologic studies, cigarette smoking does not substantially affect the associations of CHD with fine particulate air pollution[70, 83, 84] and community noise.[22, 89] Furthermore, in these analyses, neighborhood income quintiles were used to approximate individual SES. There is some evidence that this method could effectively minimize the confounding effects of individual SES.[170, 171] Overall, based on available evidence, those unmeasured factors were less likely to substantially affect the observed associations of CHD mortality with traffic proximity, traffic-related air pollution, and community noise.

Second, the exposure assessment was based on residential postal codes of study subjects to approximately estimate residential exposures to traffic-related air pollution and

community noise. As in previous studies, this method could not precisely reflect actual individual exposures[52, 190] because some environmental factors including surrounding buildings,[172] wind direction,[62] and housing characteristics (indoor infiltration of outdoor fine particles may vary from 40 to 70%)[51] as well as individual factors such as the time spent at home,[52, 222] indoor air pollution and noise levels,[25, 224] window orientation of living room and bedroom,[97, 222] and occupational exposure[92, 98] might substantially affect actual individual exposure. Nevertheless, these unmeasured factors were likely to cause non-differential exposure misclassification, leading to underestimations of true risk of coronary mortality associated with exposure to traffic-related air pollution and noise.[190]

Finally, the accuracy of the noise exposure assessment was strongly dependent on the availability of raw data on various transportation attributes. In some areas of the study region, required information such as road traffic volume data and surrounding building data was not available, the missing data and approximate data might introduce measurement errors in the noise exposure assessment. In addition, for the LUR models, R^2 ranges from 0.52 to 0.62, which were similar to those of previous studies.[44] These data indicate that the LUR models could only approximately estimate residential exposure to traffic-related air pollution. Improving the performance of LUR models in air pollution exposure assessment is an important research question that deserves further attention.

6.4 New Findings and Policy Implications

This research also suggests some implications for policy-making in environmental health related to traffic pollution.

First, the analyses found that living close to major roads was associated with an increased risk of CHD mortality and that changes in residential proximity to major roads were associated with an altered risk of CHD mortality: moving closer to major roads was associated with a risk similar to those consistently living close to major roads, whereas moving away from major roads was associated with a decreased risk compared with those consistently living close to major roads.[174] These findings suggest that future transportation and community planning should consider adverse cardiovascular effects associated with exposure to traffic-related pollution. Increasing distances between major roads and residential areas (e.g. > 150 m) could effectively reduce the risk of coronary mortality. In addition, the analyses confirmed that residence relocation may lead to exposure misclassification, which may bias effect estimates toward the null. Most previous relevant epidemiologic studies have not taken residential history into account, and therefore might underestimate the true cardiovascular risk associated with exposure to traffic-related pollution.

Second, the analyses found that black carbon, an indicator of the traffic-related fine particulate air pollution, was an independent risk factor for CHD mortality.[162] In most metropolitan areas, black carbon is mainly emitted from incomplete combustion of diesel fuels, and also emitted from other sources such as gasoline-powered vehicles.[29] To reduce adverse cardiovascular effects associated with exposure to traffic-related black carbon, diesel- and gasoline-powered vehicles could be restricted in densely populated urban areas.

Third, the analyses found that community noise was also an independent risk factor for CHD mortality.[223] Additionally, convincing evidence indicates that community noise may cause annoyance, sleep disturbance, and psychological stress.[25] In metropolitan areas, road

traffic is the dominant source of community noise. Worldwide, road traffic noise has been increasingly regarded as an important public health problem.[25, 27, 148] Therefore, multiple measures should be taken to reduce traffic noise emissions. In addition to greater distances between major roads and residential areas as discussed above, noise barriers, low-noise road surfaces, and speed limits (e.g. < 30 km/h) in residential areas and during the evening and night could effectively reduce road traffic noise pollution.

Fourth, traffic-related air pollution and traffic noise are two aspects of one problem – road traffic, which consists mostly of conventional diesel- and gasoline-powered vehicles. Conversely, electric vehicles do not cause air pollution, and produce far less noise pollution. Therefore, electric transportation should be encouraged, this is particularly important for public transportation such as city buses. In populated metropolitan areas, underground transportation systems should also be developed as these would reduce public exposures to both traffic noise and air pollution.

Finally, metropolitan Vancouver has relatively good air quality, the annual average $PM_{2.5}$ concentration was approximately 5 $\mu g/m^3$, which is substantially lower than that in metropolitan areas of the United States (14 $\mu g/m^3$).[70] The present research conducted in this clean urban area found a clear increase in coronary mortality associated with exposure to elevated traffic-related fine particulate air pollution. This finding supports the recent American Heart Association Scientific Statement that there is no discernable safe threshold (e.g. the United States National Ambient Air Quality $PM_{2.5}$ Annual Standard 15 $\mu g/m^3$) below which particular air pollution was not associated with excess cardiovascular risk.[11] From public health perspectives, it appears unlimited that lowing traffic-related fine particulate air pollution could reduce heart disease risk. Meanwhile, although there is a lack

of information on the exposure response relationships between noise and heart disease risk, it is plausible that lowing noise exposure could reduce psychological stress, and subsequently reduce heart disease risk.

6.5 Future Work

As discussed above, there are some limitations to these analyses. Future research should be considered to address these limitations.

First, in these analyses, some individual cardiovascular risk factors such as cigarette smoking were not available and thus could not be controlled in the data analysis. Although previous studies found that cigarette smoking did not substantially affect the associations of coronary mortality with fine particulate air pollution and community noise, it is not certain that the observations are also applicable to the population of metropolitan Vancouver. To address this concern, more detailed investigations are warranted. For example, a random sample (e.g. 5000 subjects) may be drawn from this population and be followed for a certain period of time. Individual socioeconomic, behavioral, dietary, and anthropometric data, as well as serum biochemistry data and health information may be collected. The influence of major cardiovascular risk factors on the observed associations could be examined in more detail.

Second, cellular and molecular mechanisms for the observed association between black carbon and coronary mortality should be examined to confirm that the association is biologically plausible. Pathophysiological effects of black carbon such as oxidative stress (e.g. vitamins A, E, C), inflammatory response in the lung (e.g. interleukin-6) and the systemic circulation (e.g. C-reactive protein), coagulation status (e.g. fibrinogen and

platelets), cardiac autonomic function (e.g. heart rate variability), vasoconstriction, and vascular and endothelial dysfunction should be examined. In addition, it is also important to examine the quantitative relationships between exposure to different levels of black carbon and the severity of atherosclerosis indicated by carotid intima-media thickness and coronary artery calcification.

Third, controlled exposure studies in healthy human volunteers should be performed to examine the effects of acute and chronic exposure to community noise on autonomic nervous system (e.g. heart rate, systolic/diastolic blood pressure, and heart rate variability), endocrine system (e.g. cortisol and catecholamines), and arterial vasoconstriction (e.g. coronary/brachial artery diameter).

Finally, in these analyses, black carbon was identified as an independent risk factor for coronary mortality. In metropolitan areas, the vast majority of black carbon emissions are from diesel- and gasoline-powered vehicles. Therefore, it would be interesting to perform a community-based air pollution intervention trial to reduce the concentrations of black carbon. For example, restrictions on diesel and gasoline-powered vehicles could be applied in a densely populated central city area, and the short- and long-term effects of such an intervention on ambient air quality and public health could be evaluated.

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