OCCUPATIONAL NOISE EXPOSURE AND THE RISK OF DIABETES, RHEUMATOID ARTHRITIS, AND CARDIOVASCULAR DISEASE

by

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Abstract

Occupational noise exposure is associated with an increased risk of cardiovascular disease. A biological model explains this association through a general stress reaction and the dysregulation of otherwise normal psychoneuralhormonal pathways. Given this evidence and the hypothesized link between stress and metabolic disorders or immunologic response (i.e. inflammation) we hypothesized that risk of diabetes and arthritis are elevated in those exposed to noise at work.

Cases and controls were drawn from the National Population Health Survey (NPHS), a longitudinal survey conducted by Statistics Canada. Eligible subjects were aged 18 to 55 in the first cycle (1994/1995) and who did not have the health outcome of interest up to and including the fourth cycle (2000/2001). Cases were determined from self reports in the fifth (2002/2003) through eighth cycle (2008/2009); each case was matched to five controls who were disease free at the time when the case was diagnosed. Subjects' noise exposure at work was assessed using cumulative exposure. Noise levels by various occupations/industries were derived from a job exposure matrix built from WorkSafeBC's noise exposure dataset and exposure duration was estimated according to the self-reported work status in the NPHS. Conditional logistic regression was used to estimate the odds ratios of developing the health outcomes of interest; models were adjusted for life style factors (physical activity, smoking, drinking), socio-economic factors (education, family income), and health status factors (hypertension, obesity).

In the current study the adjusted diabetes ORs (95% CI) for medium and high exposure groups (using low exposure group as reference) were 0.93 (0.61 – 1.41) and 1.04 (0.67 – 1.59), respectively. The corresponding ORs (95% CI) for rheumatoid arthritis were 1.01 (0.56 – 1.82) and 1.07 (0.57 – 2.01). For cardiovascular disease, the ORs (95% CI) were 0.87 (0.59 – 1.28) and 0.85 (0.57 – 1.27).

We did not find evidence of an increased risk of diabetes, rheumatoid arthritis, or cardiovascular disease in those exposed to occupational noise. Possible biases in this study may explain the lack of an observed association including misclassification bias – particularly of exposure - and the

healthy worker effect. Future studies are warranted and should focus on improving exposure assessment.

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Dedication

Dedicated to my parents, the shelter and beacon of my life.

Chapter 1: Introduction

1.1 Noise in the Workplace

Noise is one of the most common hazards in the workplace globally (Nelson *et al.,* 2005). In the European Union, 28% of workers involved in a survey reported that they were exposed to occupational noise which was so loud that they needed to raise their voices to talk to others (above 85 to 90 dBA) during one quarter of their working hours (EASHW, 2000). Twenty two million (17.2%) workers in the United States of America are exposed to occupational noise at a hazardous level (Tak *et al*., 2009). The exposure situation is probably worse in developing countries due to lack of effective control methods (Morata *et al.,* 1997; Shaikh, 1996; Mukherjee *et al.*, 1995; Oleru *et al.*, 1990).

The number of noise-exposed workers in British Columbia (BC) is not known, but since the number of the workers in Canada is estimated at about 10% of that in the USA, and in British Columbia about 10% of that in Canada, a crude estimate of the number of noise-exposed workers (85 dBA or over) in BC is 220,000. From 2011 WorkSafeBC statistics, we also know that 138,818 workers had audiometric test for a Hearing Conservation Program (WorkSafeBC, 2011). So the number of noise-exposed workers in BC can be estimated as within the range of 140,000 to 220.000.

1.2 Adverse Health Effects of Noise Exposure

Adverse health effects caused by exposure to noise include noise-induced hearing loss (NIHL), sleep difficulties, annoyance, psychological stress, elevated blood pressure, and cardiovascular diseases (Nelson *et al*., 2005; Ising and Kruppa, 2004). Among these, NIHL is regarded as the most well understood and has received the most attention. As one of the most common sources of noise, occupational exposure plays an important role in causing NIHL. It is estimated that about 16% of disabling hearing loss can be attributed to occupational noise exposure (Nelson *et*

al., 2005). Although much emphasis has been placed on NIHL, there is increasing evidence of other non-auditory health effects, in particular cardiovascular disease (Gopinath *et al*., 2011; Selander *et al*., 2009; Sbihi *et al*., 2008; Babisch *et al*., 2005; Davies *et al*., 2005). Noise is known to be a potent stressor and non-auditory effects are assumed to be stress-mediated. Noise exposure triggers a stress response that in turn leads to various health outcomes. Now interest is turning to other diseases that may be stress-related, such as diabetes and rheumatoid arthritis.

1.3 Biological Basis of the Noise-Disease Association

1.3.1 Noise and Stress

The perception of sound (or noise – i.e. unwanted or harmful sound) is a complex process in which two auditory pathways are involved, one from the inner ear to the auditory cortex, and the other from the inner ear to the reticular activating system which then connects to the limbic system as well as the autonomic nervous system and the neuroendocrine system (Westman and Walters, 1981; Cohen, 1977).

In the first pathway, nerve impulses excited by sound stimuli travel along the ascending nerve path from the receptor cells in the Corti to the auditory centers in the cortex. These impulses reach the temporal lobe and are perceived and interpreted consciously. A descending nerve path also exists, from the temporal cerebral cortex to the dorsal cochlear nucleus, exerting inhibitory and some minor excitatory effects.

In the second pathway, nerve impulses are also generated at the inner ear. However, the nerve fibers branch out and connect to the motor cell nuclei subserving reflexes within the brainstem and to the reticular activating system (RAS) in the midbrain. Since the RAS is also linked to the sympathetic-adrenal neuroendocrine (SAM) system and the hypothalamo-pituitary-adrenal neuroendocrine (HPA) system, the impulses arriving at the RAS can also be conveyed to these two systems. The SAM system regulates the secretion of catecholamines, adrenaline (epinephrine) and noradrenaline (norepinephrine) while the HPA system regulates the

corticosteroids. These two systems and the hormones regulated by them play an essential role in adapting human body to stressors (discussed in detail in Section 1.3.2). Therefore, the auditory system, the central nervous system, and the neuroendocrine system are all connected by these two pathways.

The mechanism of the stress response elicited by sound acting as a stressor can be explained according to the biological basis of these "direct" and "indirect" pathways. The pathway involving the reticular activating system is regarded as the direct pathway because the sound stimuli "directly" evoke the stress response by neural activation of the reticular activating system, which in turn triggers the response of the SAM system and the HPA system. The other pathway, which connects to the cerebral cortex, is referred to as the indirect pathway because whether a sound stimulus is perceived as a stressor or not depends in part on the cognitive processing of the auditory cortex (Ising and Kruppa, 2004; Babisch, 1998; Westman and Walters, 1981).

With respect to the direct pathway, we must consider that the auditory system evolved to arouse or to provide "early warning"; thus in response to sound it activates the reticular activating system automatically and in turn the autonomic-neuroendocrine responses. This "defense" mechanism works unconsciously. In the indirect pathway, it is a person's cognition of the perceived sound/noise that determines the degree of stress generated by the sound stimuli and this is influenced by both situational parameters (e.g. communication tasks, requirement of concentration) and individual parameters (e.g. coping potential, noise sensibility, attitude towards the sound/noise) (Ising and Kruppa, 2004).

The activation of two pathways is not mutually exclusive. They work simultaneously when there is a sound stimulus, with one pathway predominating over the other, depending on the characteristics of the sound. The direct pathway is thought to be selected more often when the sound stimulus is of high intensity and is novel and unpredictable, while the indirect pathway is selected more often when the sound level of the stimulus is moderate but the signal contains meaningful information, or when other situational or individual parameters are involved (Babisch, 1998; Westman and Walters, 1981). The noise-stress hypothesis response is shown

graphically in **Figure 1. 1**.

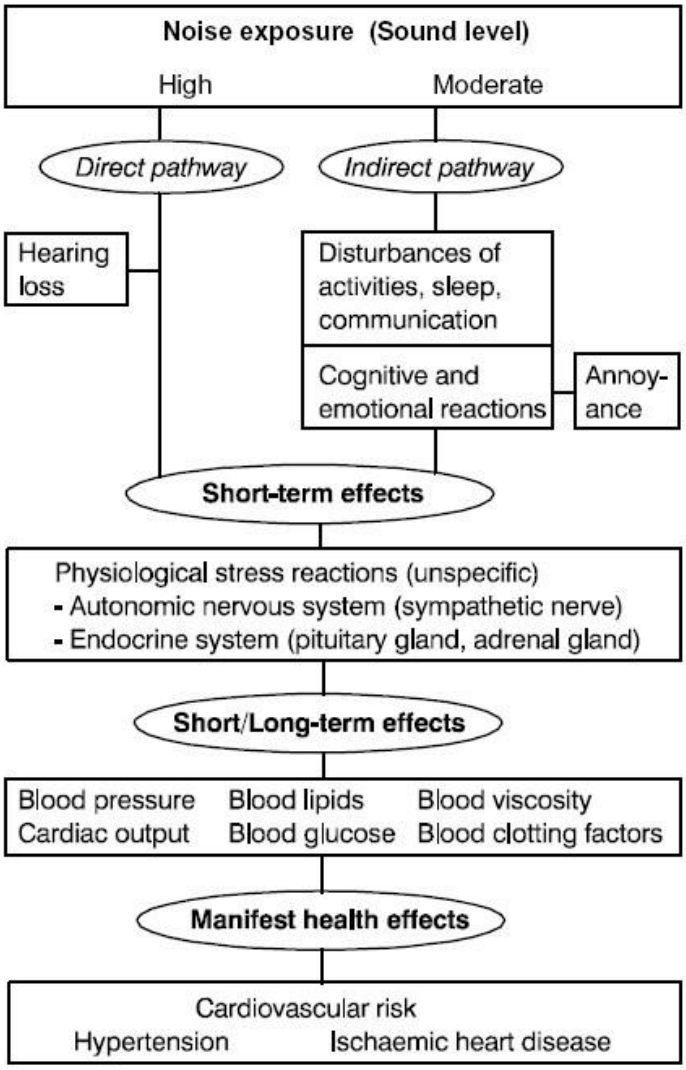


Figure 1. 1 Noise and cardiovascular risk-reaction model (from Babisch, 1998)

1.3.2 Stress Response

The general adaptation syndrome, or the stress syndrome, is a defense mechanism of the organism to cope with stress and maintain homeostasis. Many organs and systems of the body are activated to deal with stress under the regulation of the sympathetic nervous system and neuroendocrine system. In Selye's theory, the fully developed general adaptation syndrome has three stages: an alarm reaction, a stage of resistance and a final stage of exhaustion. Although the stress response exists as a protective mechanism of the organism, excessive activation of this

response will lead to adverse disease outcomes. Some severe stress rapidly results in exhaustion, or even death (Selye, 1973).

The biological basis for the stress response was explained in a model proposed by Henry (1993). In his model, two major stress reactions were identified: the defense reaction, which responds actively to cope with stress to the organism; and the defeat reaction, a passive response when the body feels loss of control. The disease outcomes associated with a stress response are thought to relate to the dysregulation of these two reactions.

Henry's defense reaction, which is equivalent to the fight or flight response, is mainly based in the SAM system. The reaction is activated when the organism's control is threatened. The sympathetic nervous system plays an essential role in this response and has a major regulating effect on the activity of smooth muscles or cardiac muscles. Through the secretion of norephinephrine, the function of the organs (e.g. heart, vessels, skin, etc), which consist of smooth muscles or cardiac muscles innervated by the sympathetic nervous system, is increased. Furthermore, the activation of the sympathetic nervous system conveys the signal to the adrenal medulla through sympathetic preganglionic fibers from spinal cord, which then causes the adrenal medulla to release norepinephrine and epinephrine. This process further strengthens the sympathetic response in target tissues or organs (Lovallo, 1997). The release of norepinephrine from locus ceruleus in the brain stem to various locations of the brain heightens the organism's sense of attention and vigilance (Dinan, 1996).

Henry's defeat reaction is activated when the organism feels loss of control and it is regulated through the hypothalamic-pituitary-adrenocortical (HPA) axis. Among the hormones (ACTH, corticosteroids, catecholamine, etc.) involved in the defeat reaction, cortisol is most important and has numerous central and peripheral effects, such as increasing plasma concentrations of amino acids and glucose, enhancing the actions of the sympathetic nervous system, and increasing the plasma volume, which are necessary for the organism to cope with stress (Vander *et al*., 1994).

1.3.3 The Noise-CVD Biological Model

Based on the hypotheses of the noise-stress and stress-physiology responses, an association between noise exposure and cardiovascular disease has been discussed (Ising and Kruppa, 2004; Maschke *et al*., 2000; Babisch, 1998).

In the defense reaction, the response of the SAM system is normally transient. Repeated or chronic activation of the system however might increase blood pressure and change the structure of the heart and vessels, which are regarded as important pathophysiological changes in the development of CVD (al' Absi and Arnett, 2000). In the defeat reaction, cortisol plays an important part and is believed to be associated with cardiovascular disease through its cardiovascular activation effect (al'Absi and Arnett, 2000).

The results from many experimental studies in both humans and animals support the proposed biological model. It was found that exposure to noise caused a significant increase in systolic, diastolic and mean arterial pressure (Andren *et al.*, 1983). In the Sudo *et al.* (1996*)* study, levels of epinephrine, norephinephrine, and cortisol were increased in subjects exposed to noise. In animal studies, Peterson *et al.* (1981) showed increased blood pressure in rhesus monkeys exposed to noise representing an occupational environment. The blood pressure did not go back to the normal level until one month after the cessation of exposure. Similar results have been found in other animals, such as rats and dogs (Fisher and Tucker, 1991; Engeland *et al.*, 1990; Friedman *et al.*, 1967).

It was proposed that, between the two pathways of noise perception, the indirect pathway is selected more frequently when the noise intensity is low and contains content and meaningful information, or when other parameters are involved. On the other hand, if the noise exposure is of high intensity or novel to the receiver, the direct pathway may be the major path. It is unknown which of the two stress reactions is activated more frequently by which pathway. It is possible that either pathways may be related to either reaction and there are complex interactions between the pathways and stress reactions.

1.3.4 A More General Biological Model

As discussed, two major stress reaction patterns are activated in stress response and may result in cardiovascular effects. However, the impact of the stress response is not restricted to the circulatory system. Many other organs or systems are involved, working together to adjust the organism to either external or internal stress, such as the nervous system (increased arousal, cognition, and vigilance), respiratory system (more air intake for increased metabolism), and digestive system (inhibited function). Therefore, excessive activation of the stress response and subsequent dysregulation of normal systems may impact various parts of the body, not just the cardiovascular system, and lead to other disease outcomes, for example, diabetes or rheumatoid arthritis, discussed below.

1.3.4.1 Biological Basis for a Noise and Diabetes Association

Diabetes and CVD share risk factors such as obesity, physical inactivity, and hypertension. This indicates that it is possible that these diseases may share similar pathophysiologic pathways. The noise-CVD biological model discussed involves, both the SAM system and the HPA axis in the stress response caused by noise exposure, representing the defense reaction and the defeat reaction respectively (Henry, 1993). Over activation of the HPA axis can result in chronic hypercortisolism, which in turn leads to visceral fat accumulation, causing central obesity, an essential risk factor for type 2 diabetes (Chrousos, 2000). Moreover, high levels of cortisol are associated with insulin resistance and/or hyperinsulinemia, which include heightened gluconeogenesis, visceral fat cell growth, carbohydrate intolerance, increased total cholesterol, LDL, triglycerides, decreased HDL, and impaired insulin secretion. All of these are regarded as important changes in the development of diabetes (Chrousos, 2009; Chrousos, 2000; Maschke *et al*., 2000). Given the association between noise and hypertension and CVD, it is also possible that there exists an indirect relationship between noise exposure and diabetes using hypertension and/or CVD as an intermediate factor.

1.3.4.2 Biological Basis for a Noise and Rheumatoid Arthritis Association

During the stress response, the immune system is involved and its function is influenced by the stress reactions in a very complex way; whether a proinflammatory or an anti-inflammatory effect is expected largely depends upon activity of the HPA axis (Chrousos, 2009; Chrousos, 1995; Sternberg *et al*., 1992). The increased activity of the HPA axis, which results in increased levels of glucocorticoids (mainly cortisol) and catecholamines, influences the function of leukocytes and accessory immune cells and suppresses the release of proinflammatory cytokines (TNF, IL-1, IL-6, IL-8, IL-12). Therefore, a suppressed function of the immune system is expected to protect the organism from an "overshoot" of the inflammatory response.

Conversely, decreased activity of the HPA axis leads to low levels of plasma cortisol, a situation in which the function of the immune system and the inflammatory effect are heightened due to lack of suppression from the HPA axis. The activation/suppression of the HPA axis depends on many factors such as the duration of stress, the intensity of stress, the perception of stress, and the internal environment of the stressed individual (Straub and Kalden, 2009). Therefore, although there may be a biologically plausible association between noise as an external stressor and rheumatoid arthritis as an autoimmune disease, the association could be quite complex.

1.4 Diabetes

Diabetes is a chronic disease which results when either the pancreas is not able to produce enough insulin or when the body cannot use insulin effectively. Generally speaking, there are two major types of diabetes. Type-1 diabetes occurs due to lack of insulin production by the pancreas and it is more frequently diagnosed in children, teenagers, and young adults. The exact cause of the type-1 diabetes is unknown and therefore it is considered unpreventable.

Type-2 diabetes, which results from ineffective use of insulin, constitutes most diabetes cases and it is most often diagnosed in adults. The risk factors for type-2 diabetes include advanced age, overweight or obesity, physical inactivity, high blood pressure and/or high cholesterol, heart

disease, and family history of diabetes (WHO, 2012; PHAC, 2012). Due to the unknown cause of type-1 diabetes, we only focus on type-2 diabetes in the current study.

Globally, 285 million people were diagnosed with diabetes in 2010. This number is expected to increase to 438 million by 2030 (Canadian Diabetes Association, 2013). In 2004, it ranked 11th leading causes of death in the world (WHO, 2004). Within Canada, there were approximately 1.4 million people with diabetes in 2000. Ohinmaa *et al*. (2004) predicted that this number would reach 2.4 million in 2016 and the total healthcare costs for diabetes were projected to increase from $4.66 billion in 2000 to $8.14 billion in 2016. Currently Canada is facing a challenge in that type-2 diabetes is increasing dramatically for various reasons including an aging population, increasing obesity prevalence, unhealthy lifestyle, and increasing number of new immigrants from high risk populations (Canadian Diabetes Association, 2013). In British Columbia, 6.46% of the population (6.92% of men and 6.01% of women) had diabetes in 2007/2008. The prevalence of diabetes in BC has a slight increasing trend, based on longitudinal data on diabetes from 2001/2002 to 2007/2008 (Provincial Health Services Authority, 2010). In 2007, 996 deaths were caused by diabetes, 3.2% of total deaths in BC (Statistics Canada, 2007).

1.4.1 Epidemiological Studies of Noise and Diabetes

Very few previous population-based studies have investigated this topic. Only one population-based study was found that assessed the direct association between noise exposure and diabetes. Sorensen *et al*. (2012) conducted a cohort study to investigate whether long-term exposure to residential road traffic noise was associated with increased risk of diabetes. They found incidence rate ratios of 1.11 (95% CI: 1.03 – 1.19) and 1.14 (95% CI: 1.06 – 1.22) per 10 dB increase in road traffic noise at diagnosis and during the 5 years preceding diagnosis of diabetes, respectively. Besides the stress response mechanism discussed in previous sections, they proposed another possible biological mechanism associated with the sleep disturbance caused by road traffic noise leads to diabetes based on a positive association found between type 2 diabetes and deficient sleep quantity and/or poor sleep quality in previous epidemiological studies (Cappuccio *et al*., 2010). In the environmental scenario, the stress mechanism and sleep

disturbance mechanism work together and lead to the diabetes outcome. However, the sleep disturbance mechanism is less likely to play a role in the occupational scenario.

No studies were found focusing on the direct association between diabetes and occupational exposure to noise. Other studies have been conducted to investigate the relationship between work stress and diabetes, however. In Li *et al*.'s study (2012), work stress was associated with both diabetes (OR: 1.27; 95% CI: 1.02 – 1.58) and prediabetes[1] (OR: 1.26; 95% CI: 1.01 – 1.58) in men, but not women. However, Djindjic *et al*. (2012) found the opposite results; women with higher occupational stress had higher risk of diabetes compared to men. Given the inconsistency from previous studies, Cosgrove *et al*. (2012) conducted a meta-analysis of nine studies to investigate the association between work-related psychosocial stress and type 2 diabetes. The work-related psychosocial stress was evaluated in the form of high demand, poor decision latitude, poor social support, job strain, or long working hours. No evidence was found to support the hypothesized association. The author suggested future studies aim at using a more rigorous assessment of work-related stress and also including other non-work social and relationship factors as indicators of psychological stress.

To summarize, although the noise-diabetes association seems biologically plausible, there have been limited population-based studies and evidence to support this association. The results from relevant studies were inconsistent. Even though a work stress-diabetes relationship might parallel the noise-diabetes biological model to some extent, the stress caused by noise exposure can be significantly different from general work-related psychological stress due to the complex process of noise perception. Furthermore, other mechanisms may exist to explain the association between noise exposure and diabetes as proposed by Maschke *et al*. (2000) for the noise-CVD association. It is possible that noise exposure leads to behavioral changes (e.g. decreased physical activity or change of sleep habits), that then result in diabetes. Given the limited evidence and inconsistent results from previous studies, no conclusion can be made at the current stage and more in-depth studies are warranted.

[1] Prediabetes is the state in which some but not all of the diagnostic criteria for diabetes are met. People with prediabetes have glucose levels that are higher than normal but not high enough yet to indicate diabetes.

1.5 Rheumatoid Arthritis

Rheumatoid arthritis is an autoimmune disease in which the immune system attacks the body's own tissue. It influences various parts of the body, especially the joints, causing pain, stiffness, and swelling that limit the normal function of the joint. The cause of the disease is still unknown but genetic factors are thought to be involved. Women are at higher risk of RA than men while for both women and men the onset of RA is highest among people in their sixties. Besides these factors, smoking, reproductive and breastfeeding history are also associated with increased risk of RA onset (Centers for Disease Control and Prevention, 2012; Statistics Canada, 2006). Although RA seldom leads to death, severe cases seriously impact the life quality of the patient by impairing the ability to do basic daily tasks (e.g. dressing, washing) (Statistics Canada, 2006). The prevalence of RA in developed countries varies between 0.3% and 1.0%. In developing countries, there is large variation in reported RA prevalence with some lower prevalence rates similar to those reported in industrialized countries (Symmons *et al*., 2006). In 2010, 272,000 people had RA in Canada and the prevalence was 0.89%. The prevalence of RA was about two times higher in women than in men. Although the prevalence trend became relatively stable after 2006, the number of people diagnosed with RA is expected to increase to over 549,000 by 2040 (1.34% of the total Canadian population) (Arthritis Alliance of Canada, 2011). In British Columbia, 1.0% of the population (0.6% of men and 1.4% of women) had RA during 2007/2008. According to the longitudinal data from 2001 to 2008, there was an increasing trend in the prevalence of RA from 2001 to 2006 (Provincial Health Services Authority, 2010).

1.5.1 Epidemiological Studies of Noise and Rheumatoid Arthritis

A literature review of population-based epidemiological studies on the direct association between noise exposure and RA did not find any published peer-reviewed studies. Further, only one study investigating the association between stress and RA was found (using the death of a child as an indicator of psychological stress, Li *et al*., 2005). No statistically significant results were found to support the association between this severe psychological stress and RA.

Yet other pathophysiological pathways may exist beside the proposed biological model based on stress response. It is possible that noise exposure modifies risk factors (e.g. smoking status) of RA and therefore, an indirect relationship is expected (Maschke *et al.*, 2000). To better understand a potential noise-RA association, more studies are required.

1.6 Noise Exposure Assessment in Epidemiological Studies

The assessment of occupational noise exposure in epidemiological studies remains a challenge, especially for retrospective studies because the available historical exposure data is limited and no standardized method has been established. In previous studies focusing on the noise – CVD association (McNamee *et al*., 2006; Davies *et al*., 2005; Sbihi *et al*., 2003), based on which we derived the general noise – disease biological model, the noise intensity, exposure duration or the combination of the two were often used to assess occupational noise exposure.

Data on noise intensity may come from either historical or current individual noise measurements, from aggregated information from databases such as job exposure matrix (JEM), or qualitatively from self-reports of exposure. The issues with the individual level data include the limited number of measurements and the fluctuation of exposed noise level; this is more of a problem if the noise in the workplace is highly unstable and small number of measurements might not be able to capture the variation in noise level. Extrapolating current noise measurements "backward" for retrospective studies is also problematic if a temporal trend existed in exposed noise level. In addition, there may be jobs that existed historically, but no longer exist and have never been measured. By aggregating information in the JEM, these problems can be overcome to some extent. Sjostrom *et al*. (2013) estimated the validity of a JEM for occupational noise and found an 80% agreement in classifying occupational noise exposure between two groups of hygienists without systematic difference. But systematic difference was found when classifying peak level exposure.

The exposure duration is often derived from workers' work history. This information may come from either the workers' employment records or the self-reported work history. Employment records could provide a relatively objective work history but sometimes they were difficult to access. As for self-reported work history, it might not be as accurate as the employment records and is prone to recall bias and reporting bias (Brigham *et al*., 2008; Adegoke *et al*., 2004; Schuz *et al*., 2003). Using only the noise intensity to assess occupational exposure was seldom found in later studies on the noise – CVD association because the development of CVD is more of a chronic process and the exposure duration appeared to take this into consideration. A large number of recent studies used the exposure duration or cumulative exposure to assess occupational noise (McNamee *et al*., 2006; Davies *et al*., 2005; Sbihi *et al*., 2003).

Another metric used by many later studies was subjective measurement or the self-reported occupational noise, which was often derived from a questionnaire by asking 'Have you ever worked in a noisy industry or noisy farm environment?' (Gopinath *et al*., 2011) or 'Thinking of all the jobs you have ever had, have you ever been exposed to loud noise at work for at least three months' (Gan *et al*., 2011). The exposure duration was quantified from the question 'how long a period did you work in this industry?' (Gopinath *et al*., 2011). Though this metric seemed less accurate in quantifying exposure compared to the two metrics mentioned above, it did have an asset in incorporating some factors involved in the perception of noise, such as personal susceptibility. This was more likely to be the case when exposed noise intensity was moderate, in which case the indirect pathway was assumed to predominate and many situational and individual factors (e.g. communication tasks, requirement of concentration, noise sensibility, attitude towards the sound/noise) were involved. Schlaefer *et al*. (2009) studied the validity of self-reported occupational noise exposure by comparing it to the exposure estimated from a JEM. Their findings showed a high agreement between self-reported noise exposure and that derived from the JEM, especially at the noise level of 80 dBA.

Another important issue related to occupational noise exposure is the effect of hearing protectors. The influence of hearing protectors on exposure estimates is more likely to be a problem in recent years, as hearing conservation programs were introduced to protect worker's hearing in

the workplace starting about 1980. Babisch (1998) discussed the impact of hearing protectors on the results of studies focusing on occupational noise. Hearing protectors are designed to provide a reduction of 15 to 30 dBA in the perceived noise exposure (Berger, 1993). If the subject wears hearing protector at work, the measured noise level by sound level meter or dosimeter is higher than the actual noise level perceived by the subject. Therefore, it is likely that a systematic misclassification resulting in over-estimates of exposure occurs with the presence of hearing protectors. Talbott *et al*. (1996) suggested a role of hearing protectors as an effect modifier on study results and Sbihi *et al*. (2010) studied the influence of the use of hearing protector devices (HPD) in the BC lumber mill workers. Sbihi *et al*. compared the HPD-adjusted and unadjusted noise metrics on their ability to predict NIHL. They found a 4-fold increase in the noise exposure and hearing loss slope, after adjusting for HPD use. However, adjusting for the effect of hearing protectors in studies remains difficult because the status of hearing protectors use for workers is rarely known. Moreover, as the perceived noise exposure is reduced by wearing hearing protectors, the stress response becomes much more complex. When the perceived noise level decreases due to hearing protectors, the indirect pathway may dominate the potential health outcomes rather than the direct pathway. In this case, it may be the annoyance resulting from the remaining noise that triggers the stress response. This pathway is much more complex compared to the direct pathway as many other environmental or personal parameters are involved. Using a subjective exposure metric might adjust for this effect. But further studies are still needed to provide improved methodology to deal with the impact from hearing protectors.

1.7 Research Objectives

As one of the most ubiquitous hazards in the workplace, noise has the potential to cause adverse health effects in humans. Diabetes and rheumatoid arthritis are two diseases that may lead to serious outcomes and their prevalence is increasing year by year, causing increasing costs in diagnosis and treatment. Previous studies of the association between noise and CVD provide a plausible biological model that can be generalized to the association between noise exposure and these other disease outcomes. Our overarching aim therefore was to examine the association between occupational noise exposure and the health outcomes of diabetes and RA. In addition,

the noise – CVD association was examined as a sensitivity analysis to test the face validity of our findings. Specifically, the three main objectives for this thesis research were:

(1) To build a job exposure matrix for noise using measurements from WorkSafeBC's noise exposure dataset;
(2) To develop noise exposure estimates for subjects in the National Population Health Survey based on the job exposure matrix;
(3) To examine the association among the subjects in the National Population Health Survey between occupational noise exposure and risk of:
    a. Diabetes
    b. Rheumatoid arthritis
    c. Cardiovascular disease

Chapter 2: Methods

Three case-control studies were conducted nested within three sub-cohorts, representing the three health outcomes of interest. The three sub-cohorts were formed based on the original longitudinal cohort of the National Population Health Survey (NPHS). Diabetes, rheumatoid arthritis, and cardiovascular disease cases were determined from self-reports in the NPHS; each self-reported case of disease was matched to five controls who did not have the health outcome at the time the case was diagnosed. Exposure assessment was conducted by building a noise job exposure matrix, assigning the exposure level according to job titles of the subjects and cumulating exposure over self-reported time in job(s). Conditional logistic regression was used to estimate the odds ratios of developing the health outcomes of interest. Although diabetes and RA were our major concern in the study, the noise and CVD association was also assessed to test the face validity of our findings.

2.1 Background Information about the National Population Health Survey

The National Population Health Survey is a Canadian nationwide longitudinal survey established by Statistics Canada in 1994. It is conducted biennially to collect information on the health status of the Canadian population and relevant socio-demographic information, aiming to provide health-related data for both researchers and policy makers. When it was established, the NPHS included two components, a cross-sectional component and a longitudinal component. In the fourth cycle (2000/2001), the cross-sectional component was taken over by the Canadian Community Health Survey (CCHS) and the NPHS became strictly longitudinal. The longitudinal panel was composed of two components, the household component and the institution component. The institution component was terminated after the fifth cycle (2002/2003) because of large number of deaths in the original population. Therefore, the NPHS household component became the only part of NPHS that is still conducted every two years (until the final survey cycle scheduled for completion in 2014/2015; Statistics Canada, 2012). In this study, only the longitudinal household component was used.

2.1.1 Target Population

The target population of the NPHS household component was household residents of the ten Canadian provinces in 1994/1995, excluding those who lived on Indian reserves and Crown lands, residents of health institutions, full-time members of the Canadian Forces living on Canadian Forces bases, and residents of some remote areas in Ontario and Quebec. (Statistics Canada, 2012)

2.1.2 Sampling

In all provinces except Quebec, the NPHS used a stratified multi-stage sample design based on the Labour Force Survey. In Quebec, Santé Québec for the 1992–1993 Enquête sociale et de santé was used. The detailed sampling method is described in "NPHS, House Component, Cycles 1 to 9, Longitudinal Documentation" by Statistics Canada (2012). In the first cycle, 17,276 people respondents comprise the longitudinal panel. This sample size remains stable in the following cycles. Although the number of people decreased slightly from cycle to cycle due to non-response, the longitudinal sample is still representative of the 1994/1995 panel (Statistics Canada, 2012).

2.1.3 Data Collection

The data collection for the NPHS was conducted using a computer-assisted interview (CAI) system, which allowed the check of the logical flow associated with the questions being asked. This system was designed to control the validity and consistency of the data collected not only within cycle but also from previous cycles. Therefore, the quality of the information collected could be monitored and errors could be located and modified during the interview. In the first cycle, 75% of the subjects were interviewed in person and the rest by telephone. In the following cycles, telephone became the major interview method, covering 95% of the subjects. The interviewers were hired and trained by Statistics Canada to carry out surveys, especially focusing

on the content of NPHS. Many strategies were used to minimize non-response, such as assigning reasonable sample sizes to each interviewer to avoid overburden. People who refused to participate were followed up by a senior interviewer, project supervisor or another interviewer to encourage them to return to the survey. To maximize the response rate, subjects who refused to respond in some cycles were still followed up in the subsequent cycles. In each cycle, based on the outcome of the interview, the status of the subjects can be: (1) completed: subjects provided complete response to the interview; (2) deceased: subjects died during the NPHS follow-up; (3) institutionalized: subjects moved into health care institutions; (4) partial response: subjects only responded partly to the NPHS questionnaire; and (5) non-response: none of the above status was assigned. In Cycle 1, 20,095 subjects were sampled to form the longitudinal panel, and 86.0% of them participated. In the following cycles, the response rates (calculated based on the 17,276 participants in the first cycle) were: 92.8% (cycle 2: 1996/1997), 88.3% (cycle 3: 1998/1999), 84.9% (cycle 4: 2000/2001), 80.8% (cycle 5: 2002/2003), 77.6% (cycle 6: 2004/2005), 77.0% (cycle 7: 2006/2007) and 70.7% (cycle 8: 2008/2009). The subjects who refused to respond were the largest source of non-response in the NPHS while failure to trace a subject is another major source of non-response (Statistics Canada, 2012).

2.2 Background Information about the Noise Exposure Data from WorkSafeBC

Since the 1970's, WorkSafeBC, the provincial workers' compensation agency, has collected noise measurements from various industries and occupations with the last samples dating from 2004. The occupations and industries represented those with more chance of being exposed to high level of occupational noise. These samples were stored as a dataset that is available to researchers through Population Data BC (a data repository for research purposes). The variables and information contained in the dataset are listed below:

- Sampling Time: the year, month, and date when the sample was collected;
- Classification Unit (CU) Codes: internal codes used by WorkSafeBC to indicate the industry where the sample was collected;
- Job Description: the task/situation/environment where the sample was taken;

- Sampling Device Type: indicator for whether the measurement was a personal or environmental sample;
- Noise Level: noise exposure level (dBA).

2.3 Study Design

Three case-control studies were conducted, nested within three sub-cohorts from the longitudinal cohort in the National Population Health Survey defined by diabetes, rheumatoid arthritis, and cardiovascular disease. The three sub-cohorts were defined according to the inclusion criteria below:

1) Subjects must be in the age range from 18 to 55 in the first cycle (1994/1995). This criterion was used to guarantee that for each subject there were sufficient years of workplace-exposure information;
2) In the sub-cohort for a health outcome of interest, subjects must not have reported this health outcome in any of the first four cycles. For each question related to a health outcome, the answer could be yes (had the outcome) / no (did not have the outcome) or missing value (no valid information provided; see detail in Section 2.4). To minimize potential misclassification by health outcome, only those who responded "no" to the health outcome of interest for each of the first four cycles were retained in the given sub-cohort.

Follow-up started immediately after the fourth cycle (December 31 2001) and ended at the eighth cycle (December 31 2009). The starting point of follow-up was selected to balance time for estimation of the exposure duration (4 cycles prior to follow-up) with time for diseases of interest to develop (the follow-up period). The follow-up for a subject ended at the earliest of the following:

1) The subject died during the follow-up period. The NPHS provided the death year, month, and day for subjects who died;
2) In the sub-cohort for a certain health outcome of interest, a subject became a case; he or she

reported being diagnosed with the health outcome. The NPHS provided only the diagnosis year and month for diabetes and rheumatoid arthritis; therefore the diagnosis day was assumed to be the 15th of the diagnosis month. The NPHS did not provide any of the diagnosis year, month, and day for CVD, and so the diagnosis date was set to the midpoint of the two year period covered by the cycle in which the subjects reported cardiovascular disease (e.g. a subject first reported cardiovascular disease in the 6th cycle. The diagnosis time was set to December 31 2004);

3) The subject dropped out from the NPHS/was lost to follow-up.

2.4 Case and Control Definition

Cases were determined based on the self-reported disease status in the NPHS. The self-reported status of diabetes (Dinca-Panaitescu *et al*., 2012; Neutel *et al*., 2010; Ross *et al*., 2010; Millar and Young, 2003), rheumatoid arthritis (Adam *et al*., 2005), and cardiovascular disease (Chiu *et al*., 2010; Lee *et al*., 2009; Patten *et al*., 2008; Wong and Wong, 2002) in the NPHS was used in previous studies for various research objectives.

For diabetes and CVD, a case was defined as a subject with a positive response to the following questions in the NPHS: 1) “do you have diabetes?” or 2) “do you have heart disease?”

For rheumatoid arthritis, the disease status was determined based on positive response to the question: “do you have arthritis or rheumatism excluding fibromyalgia?” and identification as rheumatoid arthritis from the question “what kind of arthritis do you have (rheumatoid arthritis / osteoarthritis / other)?”

In the cohort for a certain health outcome of interest, the cases were defined at the first time they reported this health outcome during the follow-up period. For each case, five controls were randomly selected from those subjects who did not have the health outcome of interest at that time point. The cases and controls were matched on age (± 5 years) and sex.

There were 17,276 subjects in the first cycle (1994/1995) of the NPHS. According to the inclusion criteria, subjects who were less than 18 years old or older than 55 years old in the first cycle (n = 7,411) were excluded. Among those subjects aged 18 to 55 years old, 341 subjects reported being diagnosed with diabetes in the first four cycles (1994 to 2001) and 2,308 subjects were not able to provide reliable information on diabetes status for a total of 2,649 subjects excluded from the cohort. Of the eligible cohort (7,216 subjects) for diabetes, 202 new cases were reported during the follow-up period and 1,010 controls were selected (see **Figure 2. 1**). For rheumatoid arthritis, in order to avoid interference from other types of arthritis, subjects who reported *any* type of arthritis (rheumatoid arthritis / osteoarthritis / others) in the first four cycles (n = 1,879) and those who were not able to provide reliable information on arthritis status (n = 2,224) were excluded. After applying the age and disease status exclusion criteria, 5,762 subjects from the NPHS cohort were eligible for the case-control analysis of RA, among whom 91 reported rheumatoid arthritis during the follow-up period. To avoid influence from other type of arthritis, the 451 controls were selected only from those who did not report any type of arthritis in the cohort (see **Figure 2. 2**). For cardiovascular disease, among subjects aged 18 to 55 years old, 369 subjects reported CVD in the first four cycles while 2,303 people did not have reliable CVD status information, which left 7,193 subjects in the study cohort for CVD. Of these, 221 new cases of CVD were reported during the follow-up and 1,105 controls were selected (see **Figure 2. 3**).

For each sub-cohort there was a sizeable fraction of subjects (diabetes: 2,308, RA: 2,224, CVD: 2,303) whose disease status was unknown; for them the code in the disease status variable was "not stated", which is a code used by Statistics Canada to show inconsistent or not provided data.

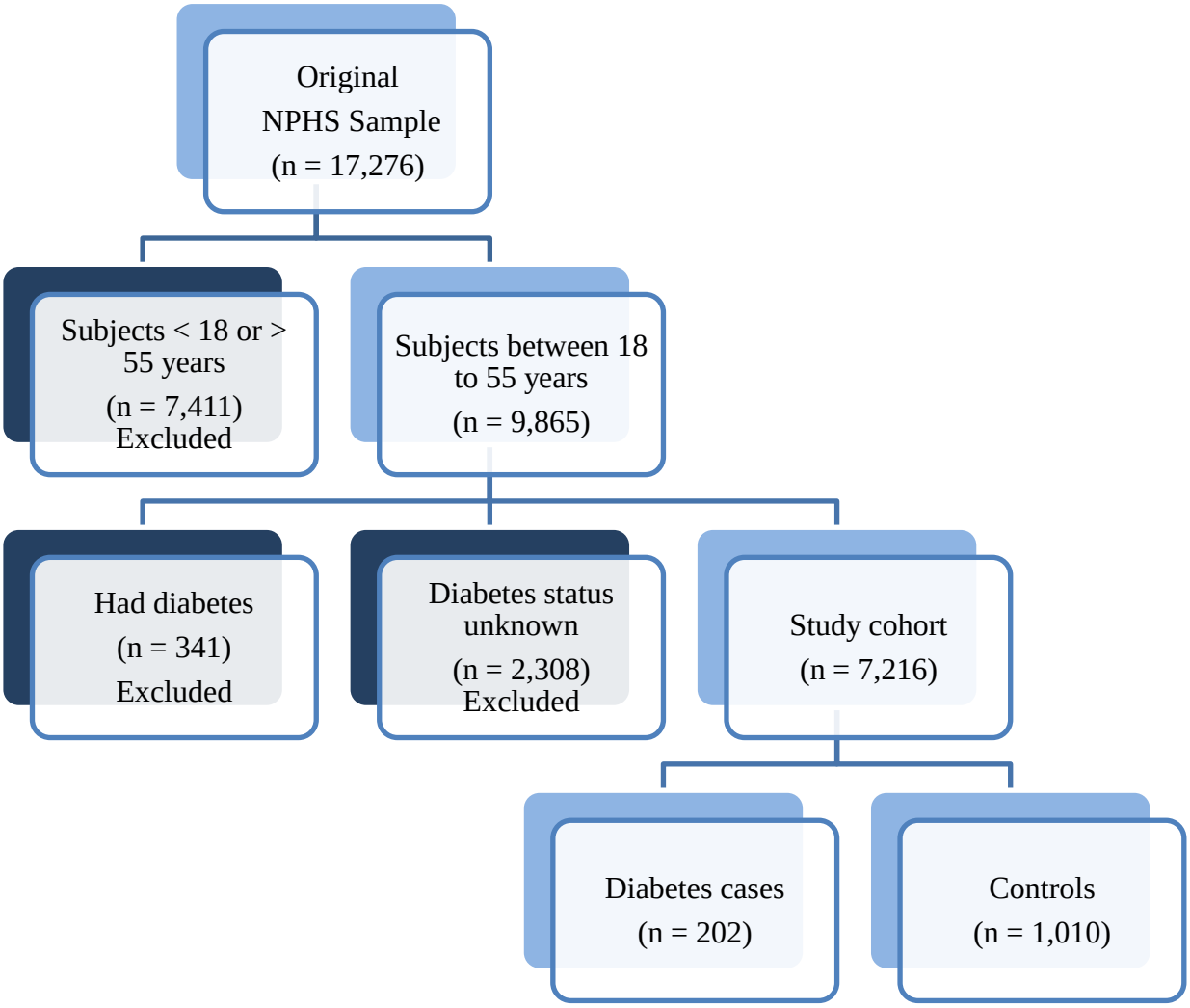
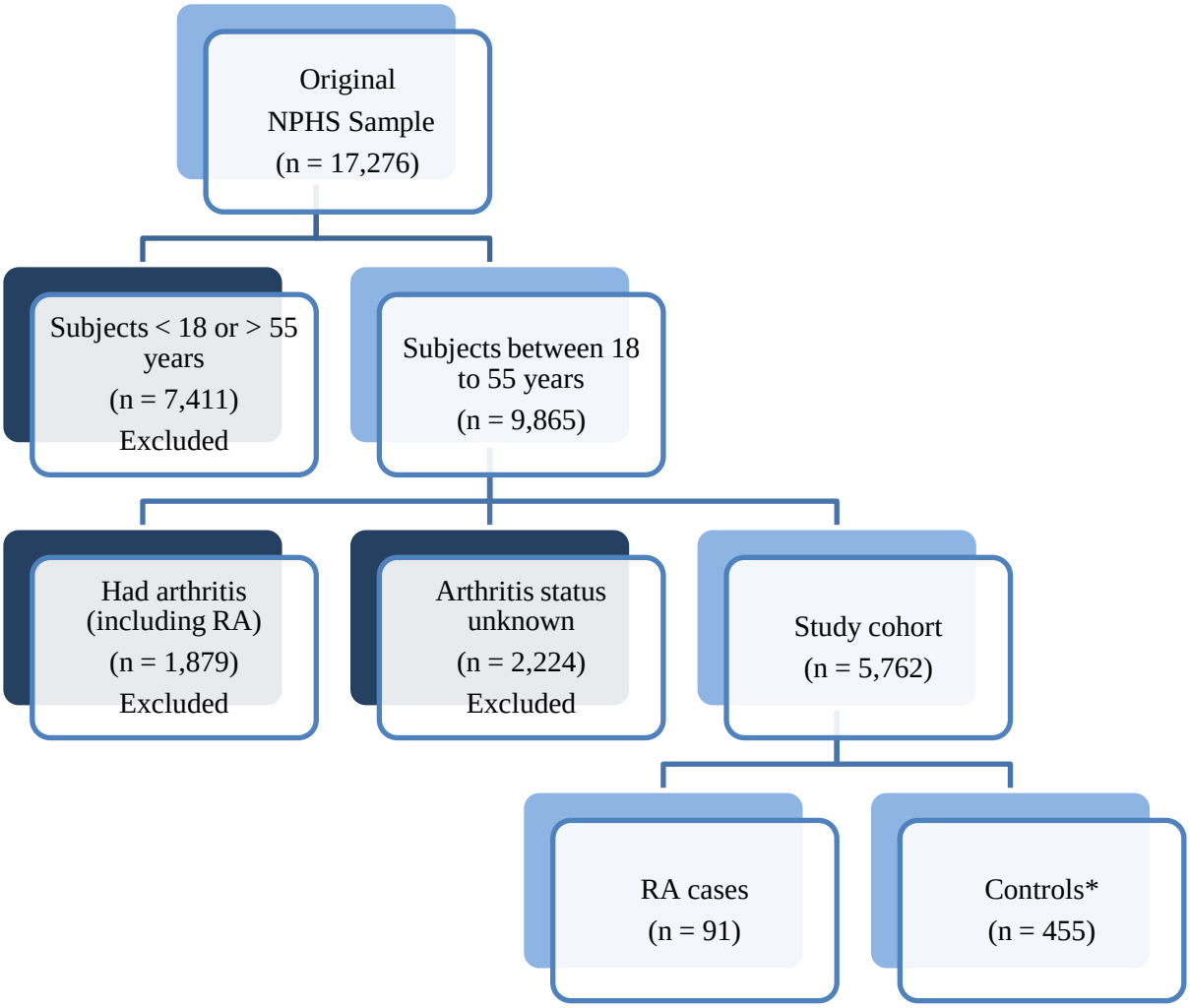


Figure 2. 1 Flowchart of Selection Cases and Controls for Diabetes



* The 455 controls only came from those who did not have any type of arthritis in the study cohort

Figure 2. 2 Flowchart of Selection Cases and Controls for Rheumatoid Arthritis

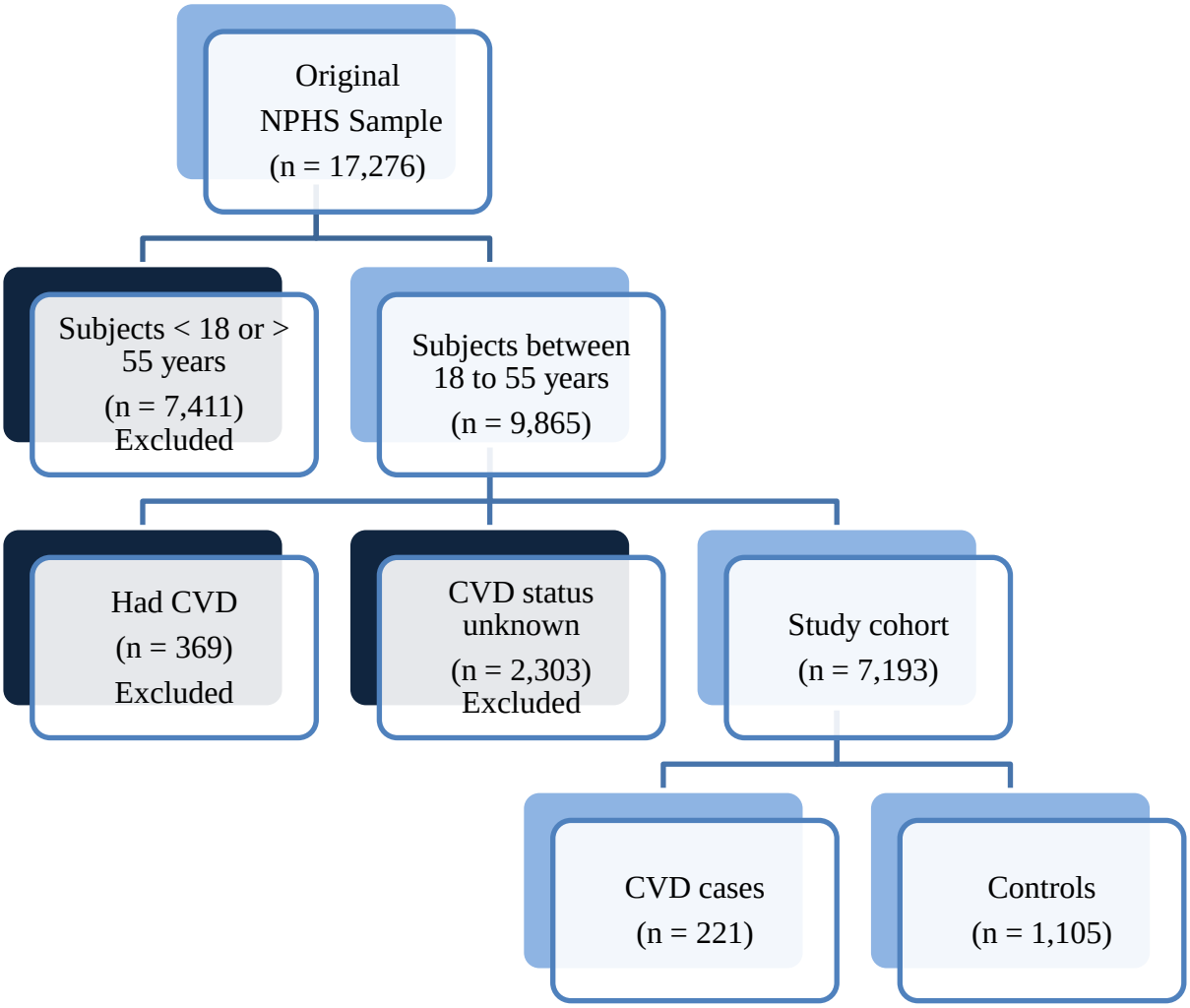


Figure 2. 3 Flowchart of Selection Cases and Controls for Cardiovascular Disease

2.5 Exposure Assessment

Occupational noise exposure for cases and controls was evaluated using cumulative exposure, the product of exposure level and employment duration for each job reported. The exposure level came from the job exposure matrix aggregated from the WorkSafeBC's noise exposure dataset and the employment duration came from the Labour Force section of the NPHS. The exposure level and duration were linked to the matrix based on the North American Industry Classification System (NAICS 2007) and National Occupational Classification for Statistics (NOC-S 2006) codes.

2.5.1 Building the Job Exposure Matrix

Job- and industry-specific noise exposure levels were obtained from the WorkSafeBC dataset. In order to link these exposure measurements to workers and their work history information in the NPHS, the CU codes (an internal industry code used by WorkSafeBC) in the WorkSafeBC data were transcribed into the standardized 4-digit NAICS (2007) codes. Using the job description and industry information provided for each exposure measurement, a corresponding 4-digit NOC-S (2006) code was assigned to each exposure measurement. To reduce error in the code assigned, an indicator variable representing the degree of confidence of assigning the right code was generated by the researcher. This variable had three values, 2 "very confident in the assigned code", 1 "some uncertainty about whether the appropriate code was assigned", 0 "do not know which code to assign and no code was assigned". Only observations having a confidence degree of 2 were kept in the dataset (about 90% of the original dataset).

After the first round of assigning the 4-digit NOC-S code, 500 observations (1.1% of all observations) were randomly selected from the dataset. The NOC-S assigning process was independently repeated for these 500 observations by a second researcher who was familiar with the NOC-S coding system to improve the accuracy of the assigned codes. When there was a dispute with the codes assigned by the two researchers, if a more appropriate code could be decided after discussion, the more appropriate code were selected and corrections were made in the whole dataset. If it was difficult to decide which code was more appropriate, no actions were made.

For each observation in the noise database, a 2-digit NAICS code and a 2-digit NOC-S code were also generated based on the first two digits of the 4-digit NAICS code and the 4-digit NOC-S code respectively. The mean noise levels of each 2-digit NAICS code, 2-digit NOC-S code, 4-digit NAICS code, 4-digit NOC-S code were calculated. If the number of observations for a combination of 4-digit NAICS code and 4-digit NOC-S code was 10 or over, the mean noise exposure level for this combination was also calculated. These calculated means were aggregated into a job-exposure matrix. The JEM representing exposure levels by NOC-S and

NAICS classifications was used to assign noise exposure levels to workers based their self-reported work histories in the NPHS.

Besides these calculated mean levels, there were occupations that had very little probability of being exposed to occupational noise. These occupations were identified in the NOC-S coding system and assigned a '0' level[2], and these were also added into the JEM. In the final JEM, there were three variables, the NOC-S codes, the NAICS codes and the noise levels. A sample of the JEM is shown in

Table 2. 1 and the summary information about the JEM is shown in

Table 2. 2. There were 1079 lines in the JEM and approximately 33% of the noise levels were at the most detailed level of the combination of both 4-digit NOC-S and 4-digit NAICS codes.

2.5.2 Estimating Exposure Duration

The NPHS surveys were conducted biennially so that each cycle represented a two year time period. Although the interviews for each cycle could have been conducted at any time over the two year period, it was assumed that all the interviews were conducted at the midpoint of each two year period (e.g. the interviews for the first cycle were conducted at December 31st 1994, etc.). The information necessary for estimating the exposure duration was provided in the Labour Force section of the NPHS. The Labour Force section asked the subjects about information related to their occupations one year prior to the interview. Therefore no data was provided for job status in the second year of cycle and this had to be inferred. To estimate the exposure duration, three variables were derived from the NPHS Labour Force section:

HOUR: the total number of hours the subject worked per week in the past year, estimated from the following question "About how many hours a week do you usually work at your job? If you

[2] In reality the exposed sound levels for these "unexposed" occupations might range from 40 to 60 dBA and could not possibly be 0. However, when calculating the cumulative noise exposure, because of the log scale the difference between 0 and 40 to 60 dBA will not have significant influence on the categorization of noise exposure. So the '0' level was used for convenience, and as a code for "assumed no exposure".

usually work extra hours, paid or unpaid, please include these hours";

Table 2. 1 Sample of the Noise Job Exposure Matrix, showing (i) entries of 4-digit NAICS and 4-digit NOC-S (only where n>10); (ii) 4-digit NOC-S only; (iii) 4-digit NAICS only; (iv) 4-digit NOC-S – NO EXPOSURE; (v) 2-digit NOC-S only; and (vi) 2-digit NAICS only

NOC-S	NAICS	Noise Level (dBA)
H523	**3211**	87.2
J141	**3211**	95.4
H523	**3212**	87.6
J193	**3212**	95.0
…	**…**	…
H523	**N/A**	88.0
J141	**N/A**	95.3
J193	**N/A**	94.9
…	**…**	…
N/A	**3211**	92.7
N/A	**3212**	90.0
…	**…**	…
A011	**N/A**	0.0
B011	**N/A**	0.0
…	**…**	…
H5	**N/A**	88.2
J1	**N/A**	93.4
…	**…**	…
N/A	**32**	91.7
N/A	**33**	91.9
…	**…**	…

Table 2. 2 Summary of the Composition of the Job Exposure Matrix. Number of Noise Levels in Each Category Based on Different Detail Level of NOC-S and/or NAICS Codes (the most detailed has both 4-digit NOC-S and 4-digit NAICS)

	Frequency	Percent (%)
Both 4-digit NOC-S and NAICS	362	33.55
4-digit NOC-S, no NAICS	264	24.47
4-digit NAICS, no NOC-S	132	12.23
"0" exposure 4-digit NOC-S	255	23.63
2-digit NOC-S, no NAICS	43	3.99
2-digit NAICS, no NOC-S	23	2.13
Total	1,079	100

WEEK: the total number of weeks the subject worked in the past year, estimated from the question "During the past 52 weeks, how many weeks did you do any work at a job or a business?

(Include paid vacation leave, paid maternity leave, and paid sick leave";
TWOYEAR: a variable indicating whether, within a two year period covered by each cycle, the work status one year prior to the (assumed mid-point) interview was the same as that one year after the interview. The values of the TWOYEAR variable could be:

- "0" (derived variable indicating did not work in the past 12 months and did not work at the time of the interview) the subject did not have significant occupational noise exposure in the two year period;
- "1" (derived variable indicating that subject worked in the past 12 months but did not work at the time of the interview or the opposite) the subject had one year of occupational noise exposure;
- "2" (derived variable indicating that subject worked both in the past 12 months and at the time of the interview) the subject had occupational noise exposure status over the two year period;
- "missing" (indicating that the subjects did not provide reliable information on this variable, details on dealing with missing value stated in Section 2.8.2).

The exposure duration within each two year period was calculated using the following formula:

$$\text{EXPOSURE DURATION (years)} = (\text{HOUR} * \text{WEEK} * \text{TWOYEAR}) / 2000 \qquad (1)$$

where 2000 represents the working hours for a worker with a normal shift in a year (50 weeks/year, 40 hours/week). The unit of the EXPOSURE DURATION is year.

2.5.3 Assigning Noise Exposure Level

In each cycle, subjects provided a description of their job and industry in the one year period prior to the survey and based on these descriptions, a 4-digit NAICS code and a 4-digit NOC-S code were assigned by Statistics Canada. The noise exposure level in the JEM from WorkSafeBC was linked to each subject in each cycle based on the NAICS and NOC-S codes. Each subject

was assigned a noise exposure level (variable name: MEAN, unit: dBA) in each cycle, using the following assignment procedure (also **Figure 2. 4**):

1) If the combination of the 4-digit NOC-S code and 4-digit NAICS code in the NPHS could be found in the job exposure matrix, the corresponding noise exposure level was assigned. Exposure periods which were assigned a noise level in this step got an "assignment confidence rank' of one to indicate these had the highest validity;
2) If the combination could not be found in the job exposure matrix, the noise exposure level was assigned only according to the 4-digit NOC-S code. An assignment confidence rank of two was given to exposure periods assigned a noise level in this step;
3) If the job exposure matrix did not have the exposure level for the 4-digit NOC-S code in NPHS, then the noise exposure level was assigned based on the 4-digit NAICS code. Exposure periods which got a noise level in this step were given an assignment confidence rank of three;
4) The noise levels assigned in the first three steps all came from the available information from the JEM. Priority was given to them over the zero exposure occupations determined by expert judgment. After the first three steps, there were still some subjects who did not have a corresponding noise exposure level. According to their NOC-S codes, a portion of these subjects were assigned a zero exposure based on expert judgment because their job in that cycle had very little probability of being exposed to occupational noise. Subjects who were assigned a noise level in this step got a rank of four;
5) Among the subjects left from the previous four steps, the noise exposure level was assigned at the 2-digit NOC-S level. A rank of five was given to subjects who got a noise level in this step;
6) If the job exposure matrix did not have the exposure level for the 2-digit NOC-S code in subjects in the step 5, the noise exposure level was assigned according to the 2-digit NAICS code. Subjects who were assigned a noise level in this step got a rank of six.

NOC-S	NAICS	Noise Level (dBA)	Rank
H523	3211	87.2	1
J141	3211	95.4	1
H523	3212	87.6	1
J193	3212	95.0	1
.....	.....	.....	.....
H523	N/A	88.0	2
J141	N/A	95.3	2
J193	N/A	94.9	2
.....	.....	.....	.....
N/A	3211	92.7	3
N/A	3212	90.0	3
.....	.....	.....	.....
A011	N/A	0.0	4
B011	N/A	0.0	4
.....	.....	.....	.....
H5	N/A	88.2	5
J1	N/A	93.4	5
.....	.....	.....	.....
N/A	32	91.7	6
N/A	33	91.9	6
.....	.....	.....	.....

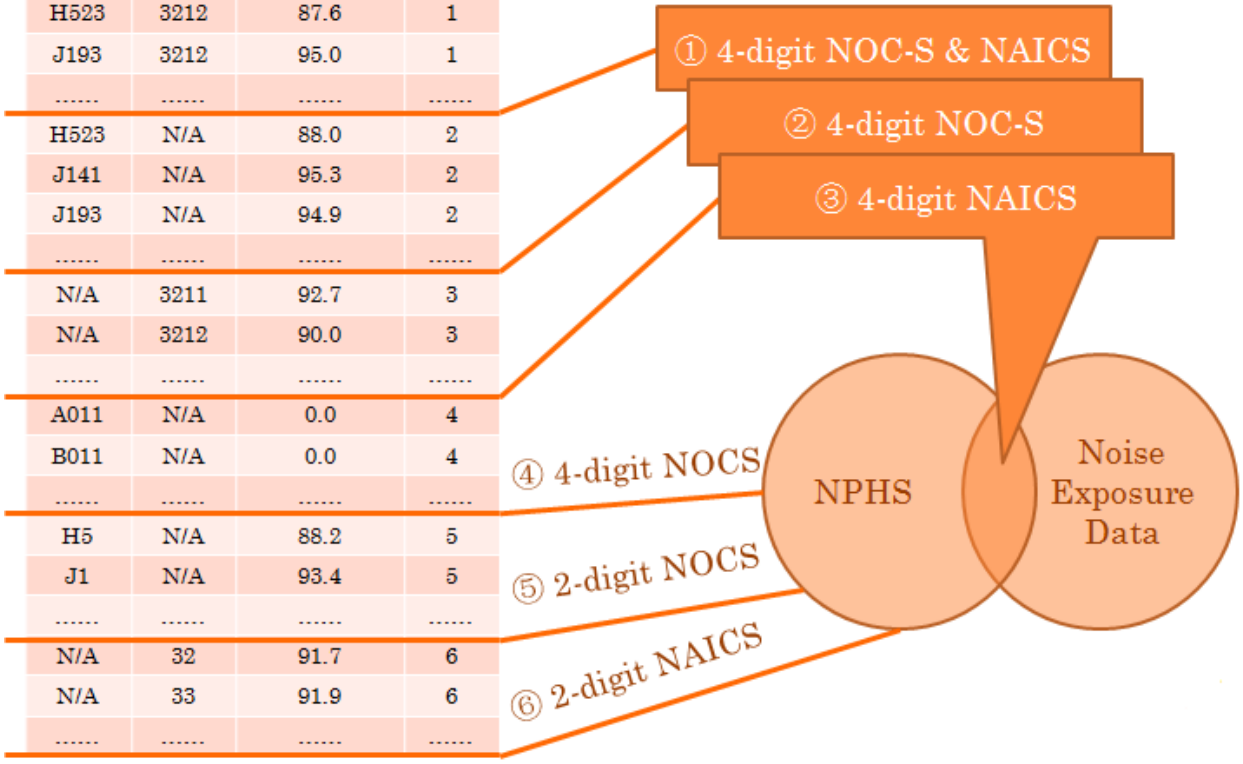


Figure 2. 4 Noise Assignment Procedures – note (4) refers to 4-digit NOC-S that are unexposed

2.5.4 Calculating the Cumulative Noise Exposure

The entire exposure period for each subject starts from the first cycle (1994/1995) to the end of follow-up. Within each two year period represented by each cycle, both the noise exposure level (MEAN) and the exposure duration (from HOUR, WEEK, TWOYEAR) were known. The total cumulative noise exposure (CNE) was estimated by adding up the cumulative noise exposure from all the cycles within the entire exposure period. The detailed formula is shown below:

$$\text{CNE} = 10\log \times [\sum_{i=1}^{n}(10^{\text{EXPOSURE LEVEL i}/10} \times \text{EXPOSURE DURATION i})] \qquad (2)$$

where i denotes the ordinal number of the cycle. The unit of CNE is dBA-years.

2.5.5 Categorizing Exposure Groups

Subjects were divided into three exposure groups as low, medium, high exposure using cut points of 85 dBA-year and 95 dBA-year. The cut points were selected based on the distribution of the calculated cumulative noise exposure and to ensure that there were enough subjects distributed in each exposure category.

2.6 Covariates

Factors that could be potential confounders or effect modifiers of the relationship between noise exposure and each disease outcome were identified according to the existing literature and then included in the analysis, as outlined below. The subjects' status for all these variables (except high blood pressure) came from the last cycle during the follow-up period to use the most up-to-date data, and were treated as constant in the analysis.

2.6.1 Income and Education

Lower social-economic status (e.g. education, income, occupation) is associated with an increased risk of diabetes (Maty *et al*., 2005; Mokdad *et al*., 2000), RA (Kwon *et al*., 2012), and CVD (Johnson-Lawrence *et al*., 2013; Beebe-Dimmer *et al*., 2004). Income and education are two important components of socio-economic status. Previous studies indicated that they were correlated with occupational noise exposure (Gan *et al*., 2011). Therefore, they were treated as confounders in previous studies focusing on noise and disease association and their effect was adjusted in the regression model (Sorensen *et al*., 2012, Gan *et al*., 2011, Selander *et al*., 2009, Wang *et al*., 2000).

The income information was obtained from the household income variable in the NPHS. In the original dataset the total household income was collapsed into deciles. In this study, the total household income was re-categorized into three categories at the cut points of $40,000 and

$80,000. The cut points were selected to ensure there were enough subjects in each category to build the regression model.

The NPHS provided several different ways to categorize the subject's education status but in the current study, the four-level categorization was used: less than secondary school graduation, secondary school graduation, some post-secondary, and post-secondary graduation.

2.6.2 Obesity

Obesity is an important risk factor for both diabetes (Maty *et al*., 2005; Mokdad *et al*., 2000) and CVD (WHO, 2013) and its effect was adjusted in the regression model of previous studies focusing on noise – diabetes and noise – CVD association (Sorensen *et al*., 2012; Gan *et al*., 2011; Gopinath *et al.*, 2011; Selander *et al*., 2009; McNamee *et al.,* 2006). For RA, the effect of obesity as a confounder was explored in our study as we speculated that being obese might increase the burden and damage of joints. Also having obesity status might prevent the subjects from participating in certain occupations, which would be associated with their noise exposure. Obesity status was derived from the Body Mass Index (BMI) of each subject using the international standard recommended by Health Canada and the World Health Organization (Health Canada, 2005). The BMI was calculated according to the height and weight of the subject using the following formula:

$$\text{BMI} = \text{Weight (kg)} / (\text{Height (m)})^2 \qquad (3)$$

The international standard BMI classification system for adults aged 18 or over had six categories: "Underweight" BMI <= 18.5; "Normal Weight" BMI 18.5 – 24.9; "Overweight" BMI 25.0 – 29.9; "Obese Class I" BMI 30.0 – 34.9; "Obese Class II" BMI 35.0 – 39.9; "Obese Class III" BMI $\geq$ 40.0.

To avoid small number of observations in some categories (Statistics Canada has a policy on releasing results with small number in certain categories), the "Underweight and Normal Weight" were merged into one category for all three health outcomes of interest. For the health outcomes of cardiovascular disease and rheumatoid arthritis, the three different classes of obese were merged into one category due to small numbers.

2.6.3 Physical Activity

Physical inactivity is another risk factor for both diabetes (Maty *et al*., 2005; Mokdad *et al*., 2000) and CVD (WHO, 2013) so its effect was adjusted in the regression models of previous studies (Sorensen *et al*., 2012; Gan *et al*., 2011; Gopinath *et al.*, 2011; Selander *et al*., 2009). Though there was no previous study on the confounder effect of physical activity on the noise – RA relationship, we studied it in the current study as being highly physically active might damage the joints and physical activity may be to some extent associated with the subjects' occupation. The subjects' physical activity status was determined based on the physical activity index, which was derived from Energy Expenditure (EE). EE was calculated according to the frequency and time per session of physical activity as well as its energy cost, the metabolic energy cost expressed as a multiple of the resting metabolic rate. The EE value for all activities in a day was calculated as follows:

$$\text{EE (kcal/kg/day)} = \text{Sum of } ((N_i \times D_i \times \text{MET value}) / 365) \qquad (4)$$

Where N_i was the number of times a respondent engaged in an activity$_i$ over a 12 month period, D_i was the average duration in hours of the activity$_i$, and MET was the energy cost of the activity expressed as kilocalories expended per kilogram of body weight per hour of activity (kcal/kg per hour) / 365 (to convert yearly data into daily data). Based on the calculated EE, the subjects' physical activity was divided into three categories: "Active" EE $\geq$ 3.0; "Moderate" 1.5 $\leq$ EE < 3.0; "Inactive" EE < 1.5 (Statistics Canada, 2012).

2.6.4 Smoking

Smoking is regarded as the risk factor for both RA (Oliver and Silman, 2006) and CVD (WHO, 2013) and was treated as a confounder in previous studies (Li *et al*., 2012; Gan *et al*., 2011; Gopinath *et al.*, 2011; Selander *et al*., 2009; McNamee *et al*., 2006). Its confounding effect was also indicated in studies focusing on the direct association between noise and diabetes (Sorensen *et al*., 2012). In NPHS, six types of smokers were defined: daily smoker, occasional smoker but former daily smoker, always an occasional smoker, former daily smoker, former occasional smoker, never smoked. The six types were re-categorized for the analysis. The "daily smoker", "occasional smoker but former daily smoker", and "always occasional smoker" were merged into one category "current smoker". The "former daily smoker" and "former occasional smoker" were merged into one "former smoker" while the "never smoked" remained the same. Therefore in this study, three types of smoker were defined: "Current Smoker", "Former Smoker", and "Never Smoked".

2.6.5 Drinking

It was suggested in some previous studies that drinking might confound the noise – diabetes association and noise – CVD association (Sorensen *et al*., 2012; Gan *et al*., 2011). In our study, four categories of drinker were used based on the types of drinkers defined in the NPHS: "Regular Drinker[3]", "Occasional Drinker[4]", "Former Drinker", and "Never Drank". In this study, the "Occasional Drinker" and "Never Drank" were merged as one due to limited number of subjects in these categories and similar risk.

[3] The frequency of drinking alcohol beverage for a regular drinker ranged from once a month to 4 to 6 times a month.

[4] Occasional drinker were people who drank less than once a month.

2.6.6 High Blood Pressure

High blood pressure is an important risk factor for both diabetes and CVD (PHAC, 2012; PHAC, 2009) and its effect was considered in the models in the current study. Two categories were defined as yes or no for: “do you have high blood pressure?”.Considering the fact that hypertension might be an intermediate factor between noise exposure and CVD, the subjects’ hypertension status was obtained from the only first cycle, i.e. we assumed that high blood pressure after the first cycle might be due to noise exposure. This did not necessarily avoid this problem, however, as noise exposure prior to the first cycle was unknown.

2.6.7 Covariates for the Three Health Outcomes of Interest

The inclusion of the covariates for income, education, physical activity, obesity, smoking status, drinking status and high blood pressure varied depending upon the health outcome under investigation, and the available evidence of an association with the health outcomes, and is summarized in **Table 2. 3**.

2.7 Statistical Analysis

The data analyses were conducted using STATA, version 10.0.

2.7.1 Descriptive Statistics

The descriptive statistics on noise exposure and covariate status for cases and controls were calculated using cross-tabulations. Since the variables for exposure groups and covariates were all categorical variables, the Pearson chi-square test and the Fisher’s exact test were used to compare whether the distributions of variables differed between cases and controls. Differences were considered significant when p-value < 0.05.

2.7.2 Bivariate Analysis

Bivariate analysis was conducted: (1) to provide a general view of the association between exposure and covariates (using Pearson chi-square test and the Fisher's exact test; (2) to see whether exposure variable or covariates were associated with the health outcome (using simple conditional logistic regression); and (3) to check the collinearity between two covariates (using Spearman's correlation coefficient).

2.7.3 Multiple Logistic Regression Analysis

To obtain adjusted odds ratios for different exposure groups, three multiple conditional logistic regression models were built, one each for the three health outcomes of interest. The multiple regression model was built with the exposure variable as the primary predictor and other covariates to control for potential confounding. The likelihood ratio test was used to test the hypothesis that all the variable coefficients in the model were equal to zero while the Wald test was used to test the significance of each single predictor in the model.

2.7.4 Selection of Predictors

The selection of predictors for the multiple conditional logistic regression model was conducted using a manual forward stepwise method. Specifically, the process started with the noise exposure group variable as the only predictor. The socioeconomic variables, education and family income, were forced to enter the model because they were the *a priori* confounders in epidemiological studies. Other covariates were then added into the model one at a time to see their influence on the ORs of different exposure groups. If adding a predictor resulted in significant change in ORs (10% or more), the predictor was regarded as a confounder and remained in the model. If adding a predictor had a minor effect on the ORs but this predictor was an *a priori* confounder or risk factor of the health outcome of interest in previous studies, it was also retained in the model. After this selection process, adjusted ORs were reported according to

this final model.

Table 2. 3 List of Covariates for Different Health Outcomes

Disease Outcome	Variable	Variable Values
Diabetes	Obesity	Underweight or Normal weight / Overweight / Obese I / Obese II / Obese III
	Physical Activity Index	Inactive/ Moderate / Active
	Type of Smoker	Current Smoker / Former Smoker / Never Smoked
	Type of Drinker	Regular drinker / Former drinker / Occasional drinker or Never drank
	High Blood Pressure	Yes / No
	Education	Less than Secondary School Graduation / Secondary School Graduation / Some Post-secondary / Post-secondary Graduation
	Total Household Income	< $40,000 / $40,000 – $79,999 / >= $80,000
Rheumatoid Arthritis	Obesity	Underweight or Normal weight / Overweight / Obese
	Physical Activity Index	Inactive/ Moderate / Active
	Type of Smoker	Current Smoker / Former Smoker / Never Smoked
	Education	Secondary School Graduation or Less / Some Post-secondary / Post-secondary Graduation
	Total Household Income	< $40,000 / $40,000 – $79,999 / >= $80,000
Cardiovascular Disease	Obesity	Underweight or Normal weight / Overweight / Obese
	Physical Activity Index	Inactive/ Moderate / Active
	Type of Smoker	Current Smoker / Former Smoker / Never Smoked
	Type of Drinker	Regular drinker / Former drinker / Occasional drinker or Never drank
	High Blood Pressure	Yes / No
	Education	Less than Secondary School Graduation / Secondary School Graduation / Some Post-secondary / Post-secondary Graduation
	Total Household Income	< $40,000 / $40,000 – $79,999 / >= $80,000

2.8 Dealing with Missing Values

Missing values were generated from the NPHS data and were categorized as follow:

Not Applicable: Some questions are only asked of people who meet certain requirements or people must respond ‘yes’ to certain questions to be asked subsequent ‘nested’ questions. For example, people who reported having a job were able to go to the questions regarding the job

description; people must respond yes to the question asking whether they have arthritis to be then asked further questions like what kind of arthritis they had. Otherwise the variable is coded as "not applicable";

Don't Know: When the subjects don't know the answer to the question, the relevant variable is coded as "don't know";

Refusal: When the subjects refuse to answer the question, the relevant variable is coded as "refusal";

Not Stated: In order to improve the quality of the collected data, consistency checks are conducted during and after the data collection process by Statistics Canada. If there is inconsistency in responses across question, corrective action is implemented by the coders of the survey. If a correction can not resolve the discrepancy, the questions involved in the inconsistency are coded as "not stated".

All the missing values in the NPHS fall into the four categories mentioned above. A subject's response falling into any of the four categories above was treated as a missing value. The detailed strategies to fill in these missing values are described in the following sections.

2.8.1 Missing Health Outcome Measurement

To avoid health outcome misclassification, subjects with missing values in the variables determining the health outcome were dropped.

2.8.2 Missing Exposure Assessment

Missing exposure data were filled through the procedures shown in **Table 2. 4**. Different procedures were applied, depending on the availability of information on the four variables necessary for estimating the cumulative noise exposure (MEAN, HOUR, WEEK, and

TWOYEAR). For example, for the seven situations belonging to category I, gaps were filled following the four steps outlined for that category in the "procedure" column. For situations in category II, CNE was calculated depending on the value of the TWOYEAR variable and for situations in category III, the population mean was assigned.

2.8.3 Missing Covariates

In the NPHS, the questions providing information on the selected covariates were asked in each cycle. Since people might not know the answer, refuse to answer, or even miss the entire cycle, in some cycles a variable might have missing values. Though the status of the covariates could change over time, it was treated as static in the study and the information on a certain covariate was obtained from the relevant variable in the cycle when the follow-up was stopped to guarantee that the information proximal to the diagnosis was used. If the variable for a certain covariate in the latest cycle had a missing value, the relevant variable in the previous cycle was checked to see if it had non-missing information on the covariate to fill in the blank. If not, then the variable in the previous cycle was referenced until the missing value was filled. If the information from the variables in all eight cycles still could not fill in the missing value, since all covariates were categorical, the category with the largest number of observations was assigned to the observations with missing value.

Table 2. 4 Procedures of Dealing with Missing Values in Exposure Assessment

Category	Variable				Procedures
	$MEAN_i$	$HOUR_i$	$WEEK_i$	$TWOYEAR_i$[c]	
I	A[a]	A	M[b]	A	1. If $NOC\text{-}S_{i-1} = NOC\text{-}S_i = NOC\text{-}S_{i+1}$, then: (1) If $TWOYEAR_i = 0 \rightarrow CNE_i = 0$ (2) If $TWOYEAR_i = 1 \rightarrow CNE_i = CNE_{i-1} / 2$ (3) If $TWOYEAR_i = 2 \rightarrow CNE_i = CNE_{i-1} / 2 + CNE_{i+1} / 2$ (4) If $TWOYEAR_i = M \rightarrow CNE_i = CNE_{i-1} / 2 + CNE_{i+1} / 2$ 2. If $NOC\text{-}S_{i-1} = NOC\text{-}S_i$ & $NOC\text{-}S_i \neq NOC\text{-}S_{i+1}$, then: (1) If $TWOYEAR_i = 0 \rightarrow CNE_i = 0$ (2) If $TWOYEAR_i = 1 \rightarrow CNE_i = CNE_{i-1} / 2$ (3) If $TWOYEAR_i = 2 \rightarrow CNE_i = CNE_{i-1}$ (4) If $TWOYEAR_i = M \rightarrow CNE_i = CNE_{i-1}$ 3. If $NOC\text{-}S_{i-1} \neq NOC\text{-}S_i$ & $NOC\text{-}S_i = NOC\text{-}S_{i+1}$, then: (1) If $TWOYEAR_i = 0 \rightarrow CNE_i = 0$ (2) If $TWOYEAR_i = 1 \rightarrow CNE_i = CNE_{i+1} / 2$ (3) If $TWOYEAR_i = 2 \rightarrow CNE_i = CNE_{i+1}$ (4) If $TWOYEAR_i = M \rightarrow CNE_i = CNE_{i+1}$ 4. If $NOC\text{-}S_{i-1} \neq NOC\text{-}S_i$ & $NOC\text{-}S_i \neq NOC\text{-}S_{i+1}$, then: (1) If $TWOYEAR_i = 0 \rightarrow CNE_i = 0$ (2) If $TWOYEAR_i = 1 \rightarrow CNE_i$ = mean CNE of population (3) If $TWOYEAR_i = 2 \rightarrow CNE_i$ = mean CNE of population (4) If $TWOYEAR_i = M \rightarrow CNE_i$ = mean CNE of population
	A	M	A	A	
	A	M	M	A	
	A	A	A	M	
	A	A	M	M	
	A	M	A	M	
	A	M	M	M	
II	M	A	A	A	(1) If $TWOYEAR_i = 0 \rightarrow CNE_i = 0$ (2) If $TWOYEAR_i = 1 \rightarrow CNE_i$ = mean CNE of population (3) If $TWOYEAR_i = 2 \rightarrow CNE_i$ = mean CNE of population
	M	M	A	A	
	M	A	M	A	
	M	M	M	A	
III	M	A	M	M	CNE_i = mean CNE of population
	M	M	A	M	
	M	A	A	M	
	M	M	M	M	

a. 'A' means the information for that variable is available;

b. 'M' means the information for that variable is missing;

c. i denotes the cycle number.

Chapter 3: Results

3.1 Job Exposure Matrix

Before data cleaning, there were 49,776 observations in the WorkSafeBC noise exposure dataset collected between 1970 and 2004. The recorded minimum and maximum noise levels were 50 dBA and 150 dBA respectively. The mean noise exposure level of the whole dataset was 91 dBA and the standard deviation was 9 dBA. There were 276 unique CU code categories and 27,867 unique job descriptions.

Based on the degree of confidence on the assigned NOC-S code, only observations that had a confidence degree of 2 were retained in the dataset (45,046 observations, 90% of the original dataset). The minimum (50 dBA) and maximum noise level (150 dBA) remained the same. The mean value and standard deviation of the noise level were 91.4 dBA and 8.8 dBA respectively. Because of the logarithmic characteristic of the decibel unit, the collected noise levels were expected to follow a normal distribution, and this was supported by the histogram and Q-Q plot of the exposure levels (**Figure 3. 1** and **Figure 3. 2**). The transformation procedure of the CU codes into 4-digit NAICS codes gave 132 different industrial categories. In terms of occupation, 264 4-digit NOC-S codes were assigned according to the job descriptions in the database.

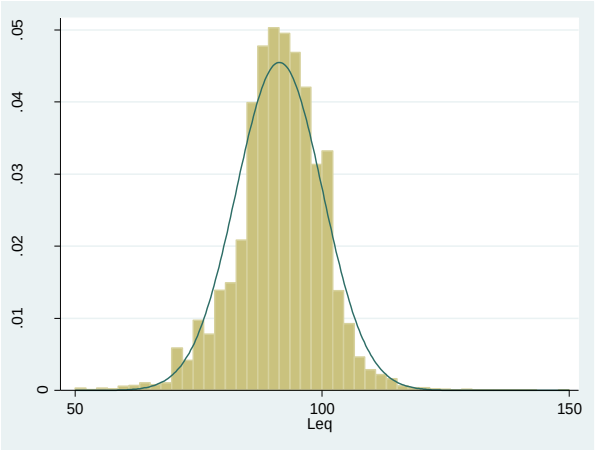


Figure 3. 1 Histogram of Noise level (N=45,046)

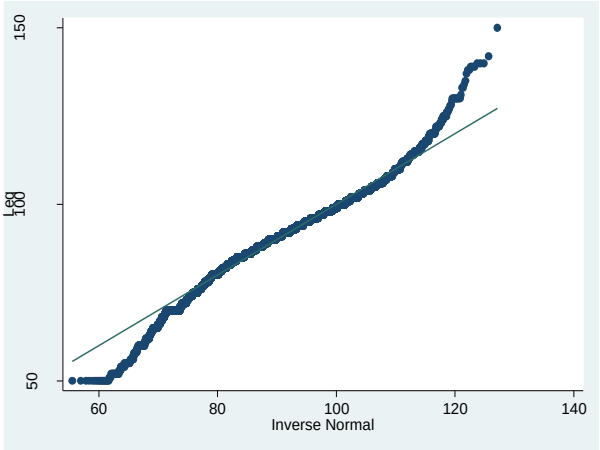


Figure 3. 2 Q-Q Plot of Noise Level (N=45,046)

3.1.1 Noise Exposure by Occupations

The noise exposure levels by occupation at the one-digit NOC-S level[5] are shown in **Table 3. 1**. Approximately 97% of all samples were collected in the following occupational categories: occupations unique to processing, manufacturing and utilities; trades, transport and equipment operators and related occupations; and occupations unique to primary industries. The highest mean noise exposure levels were also found in these three occupation groups: 92.6 dBA, 89.4 dBA, and 91.2 dBA respectively. The standard deviations of the noise levels were relatively large, especially in natural and applied sciences and related occupations (11.5 dBA).

Table 3. 1 Noise Exposure Levels by Occupations (1-digit NOC-S Level)

Occupation (NOC-S 1 digit)	Frequency	Percent (%)	Mean (dBA)	SD (dBA)
Occupations Unique to Processing, Manufacturing and Utilities	30,519	67.75	92.6	8.6
Trades, Transport and Equipment Operators and Related Occupations	10,883	24.16	89.4	7.8
Occupations Unique to Primary Industry	2,341	5.20	91.2	8.2
Sales and Service Occupations	544	1.21	81.9	8.7
Business, Finance and Administrative Occupations	218	0.48	75.8	10.7
Natural and Applied Sciences and Related Occupations	202	0.45	85.3	11.5
Management Occupations	148	0.33	74.6	8.5
Health Occupations	108	0.24	75.2	10.4
Occupations in Social Science, Education, Government Service and Religion	70	0.16	85.2	5.3
Occupations in Art, Culture, Recreation and Sport	13	0.03	84.2	5.9

[5] The noise levels are shown at one digit level for ease of presentation of the information. Otherwise the table will be too huge to show.

3.1.2 Noise Exposure by Industries

The noise exposure levels by industry are shown in **Table 3. 2** at 2-digit NAICS level. Approximately 94% of all samples were collected in the following three industries: manufacturing industry; agriculture, forestry, fishing and hunting industry; and construction industry. The mean noise exposure levels found in most industries were in the range between 80 dBA and 90 dBA, however, the highest mean noise exposure level was found in education services (92.2 dBA), followed by manufacturing (91.7 dBA), agriculture, forestry, fishing and hunting (91.1 dBA), construction (91.1 dBA), mining, quarrying, oil and gas extraction (91.1 dBA). The standard deviations of the noise levels were relatively large, especially in administrative & support, waste management, etc. (10.1 dBA).

Table 3. 2 Noise Exposure Levels by Industries (2-digit NAICS Level)

Industry (NAICS 2 digits)	Frequency	Percent (%)	Mean (dBA)	SD (dBA)
Manufacturing	37,608	83.49	91.7	8.8
Agriculture, Forestry, Fishing and Hunting	3,296	7.32	91.1	8.0
Construction	1,268	2.81	91.1	7.4
Public Administration	856	1.90	89.0	9.6
Transportation and Warehousing	569	1.26	87.8	9.7
Education Services	379	0.84	92.2	9.8
Other Services (except Public Administration)	294	0.65	87.7	6.9
Retail Trade	195	0.43	83.1	7.0
Information and Cultural Industries	135	0.30	88.3	8.5
Accommodation and Food Services	120	0.27	83.8	6.2
Health Care and Social Assistance	119	0.26	81.3	7.1
Mining, Quarrying, Oil and Gas Extraction	89	0.20	91.1	8.5
Wholesale Trade	37	0.08	83.0	9.1
Profession, Scientific, and Technical Services	20	0.04	85.9	5.2
Finance and Insurance	19	0.04	82.2	7.1
Administrative & Support, waste management, etc	17	0.04	89.8	10.1
Utilities	16	0.04	87.9	8.4
Arts, Entertainment and Recreation	7	0.02	83.1	3.5
Real Estate and Rental and Leasing	2	0.00	84.6	2.5

3.1.3 Grab Sample versus Personal Sample

Around 62 % of all samples were “grab samples” collected by sound level meter while the rest were personal samples collected by dosimeter. The mean noise levels of grab samples and personal samples were 91.4 dBA and 91.2 dBA respectively. There was only a 0.2 dBA difference between the two mean levels though the t-test showed that the difference was statistically significant (p = 0.018) because of the large sample size. (**Table 3. 3**)

Table 3. 3 Comparison between Grab Sample and Personal Sample

	Frequency	Percent (%)	Mean (dBA)	SD (dBA)	t-test
Grab Sample	28,009	62.18	91.4	9.6	p = 0.018
Personal Sample	17,037	37.82	91.2	7.2	

When comparing the noise levels collected by sound level meter and dosimeter in different occupations (1-digit NOC-S level), the differences were quite small in three occupation groups: 1) occupations unique to processing, manufacturing and utilities (0.3 dBA), 2) trades, transport and equipment operators and related occupations (0.5 dBA), 3) occupations unique to primary industry (0.2 dBA) regardless of the results of the t-test. For other occupation groups, the sound level meter always yielded a relatively lower noise level and the difference ranged between 2.9 dBA (Occupations in Social Science, Education, Government Service and Religion) to 12.0 dBA (Management Occupations). (**Table 3. 4**)

The situation for different industries (at 2-digit NAICS) was complex. The difference of the noise level between sound level meter and dosimeter methods was small in the following industries: manufacturing (0.1 dBA), agriculture, forestry, fishing and hunting (0.5 dBA), transportation and warehousing (0.4 dBA), information and cultural industries (0.6 dBA), and health care and social assistance (0.6 dBA). The difference was large and the dosimeter found a higher noise levels in the three industries: construction (1.1 dBA), retail trade (0.9 dBA), mining, quarrying, oil and gas extraction (1.9 dBA). For the following industries the sound level meter yielded a higher noise level: public administration (3.4 dBA), education services (8.9 dBA), other services except public administration (4.4 dBA), accommodation and food services (7.9

dBA), and wholesale trade (2.4 dBA); (**Table 3. 5**).

In the JEM, these differences between grab sample and personal sample were ignored because dropping the measurements collected by sound level meter meant losing the noise exposure information for a large number of occupations and industries. Both grab sample and personal sample were used to build the JEM.

Table 3. 4 Comparison between Grab Sample and Personal Sample by Occupations

Occupation (NOC-S 1 digit)	Sampling Method [a]	N	Mean (dBA)	SD (dBA)	p-value
Occupations Unique to Processing, Manufacturing and Utilities	G	19,381	92.7	9.4	0.0032
	P	11,138	92.4	7.1	
Trades, Transport and Equipment Operators and Related Occupations	G	6,279	89.2	8.8	0.0014
	P	4,604	89.7	6.2	
Occupations Unique to Primary Industry	G	1,720	91.2	8.1	0.5266
	P	621	91.0	8.5	
Sales and Service Occupations	G	198	79.4	11.6	<0.0001
	P	346	83.4	6.1	
Business, Finance and Administrative Occupations	G	150	73.9	10.6	0.0001
	P	68	80.0	9.7	
Natural and Applied Sciences and Related Occupations	G	116	82.6	12.8	0.0001
	P	86	89.0	8.1	
Management Occupations	G	97	70.5	6.8	<0.0001
	P	51	82.5	5.1	
Health Occupations	G	61	72.7	11.9	0.004
	P	47	78.4	6.9	
Occupations in Social Science, Education, Government Service and Religion	G	6	82.5	10.0	0.192
	P	64	85.4	4.7	
Occupations in Art, Culture, Recreation and Sport [b]	G	1	82.0	/	/
	P	12	84.4	6.1	

a. "G" means grab sample and "P" means personal sample;

b. T-test could not be done due to small sample size.

Table 3. 5 Comparison between Grab Sample and Personal Sample by Industries

Industry (NAICS 2 digits)	Sampling Method [a]	N	Mean (dBA)	SD (dBA)	p-value
Manufacturing	G	23,410	91.6	9.7	0.6377
	P	14,198	91.7	7.0	
Agriculture, Forestry, Fishing and Hunting	G	2,670	91.0	7.7	0.1216
	P	626	91.5	8.8	
Construction	G	306	90.2	10.4	0.0201
	P	962	91.3	6.1	
Public Administration	G	599	90.0	9.7	<0.0001
	P	257	86.6	8.7	
Transportation and Warehousing	G	392	87.9	10.8	0.6443
	P	177	87.5	6.8	
Education Services	G	312	93.8	9.8	<0.0001
	P	67	84.9	5.0	
Other Services (except Public Administration)	G	47	91.4	9.1	0.0001
	P	247	87.0	6.2	
Retail Trade	G	62	82.5	9.1	0.3668
	P	133	83.4	5.8	
Information and Cultural Industries	G	60	88.7	10.7	0.6972
	P	75	88.1	6.3	
Accommodation and Food Services	G	11	91.0	6.3	<0.0001
	P	109	83.1	5.8	
Health Care and Social Assistance	G	39	80.9	9.1	0.6693
	P	80	81.5	5.9	
Mining, Quarrying, Oil and Gas Extraction	G	59	90.5	7.7	0.3154
	P	30	92.4	10.0	
Wholesale Trade	G	19	84.2	11.6	0.4399
	P	18	81.8	5.6	
Profession, Scientific, and Technical Services [b]	/	/	/	/	/
Finance and Insurance [b]	/	/	/	/	/
Administrative & Support, waste management, etc[b]	/	/	/	/	/
Utilities [b]	/	/	/	/	/
Arts, Entertainment and Recreation [b]	/	/	/	/	/
Real Estate and Rental and Leasing [b]	/	/	/	/	/

a. "G" means grab sample and "P" means personal sample;

b. The t-test could not be conducted due to small sample size or no sample in "G" or "P" group.

3.1.4 Temporal Trend

The noise exposure level showed a decreasing trend over time but that the decrease was very slight – see scatter plot (**Figure 3. 3**). Based on the results of simple linear regression, there was a 0.15 dBA decrease every year. However, only 0.55% of the total variance in noise exposure level could be explained by year ($R^2 = 0.0055$).

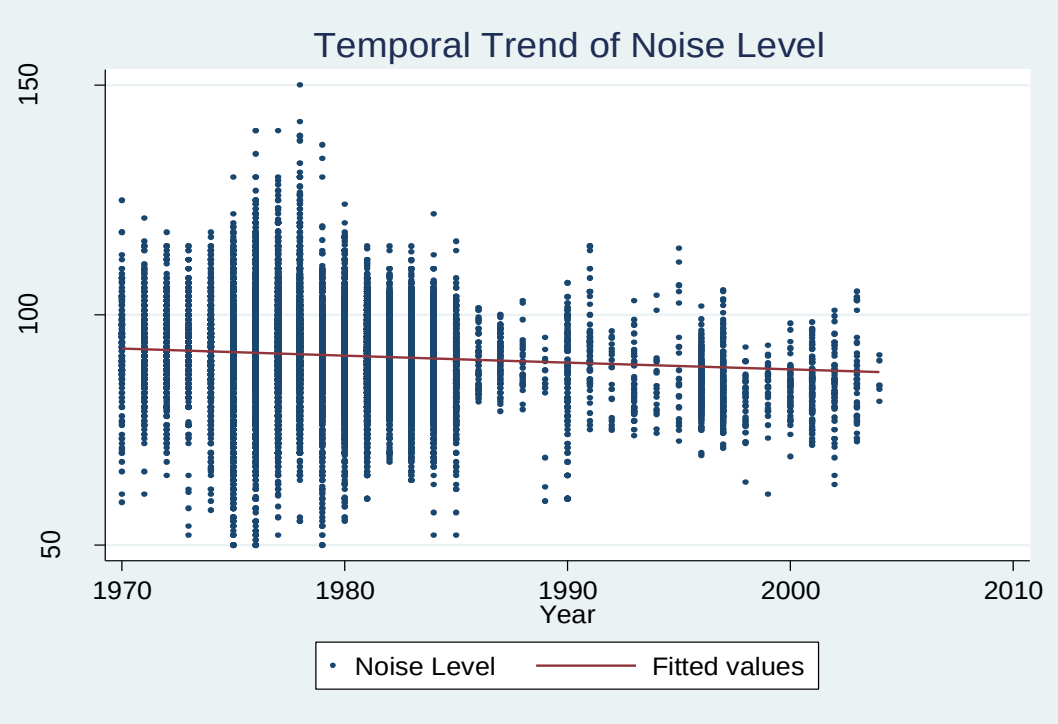


Figure 3. 3 Scatter Plot of Noise Exposure Level by Year

By visualizing the scatter plots shown in **Figure 3. 4**, there is no obvious temporal trend, neither increasing nor decreasing, found in the four groups of occupations: a. occupations unique to processing, manufacturing and utilities, b. trades, transport and equipment and operators and related occupations, c. occupations unique to primary industry, d. sales and service occupations. In all other occupation groups, the temporal trend was undetectable due to limited observations or clustered observations in certain time period (**Appendix A: Figure A. 1**).

Figure 3. 4 Scatter Plots of Noise Level in Certain Occupations

In terms of temporal trend by industries, no obvious temporal trend was found in the following three industries: manufacturing; construction; and agriculture, forestry, fishing and hunting (Figure 3.5). However, an apparent temporal trend can be seen in public administration industry. As for other industries, the temporal trend was difficult because of limited observations and clustered observation during certain time period (**Appendix A: Figure A. 2**)

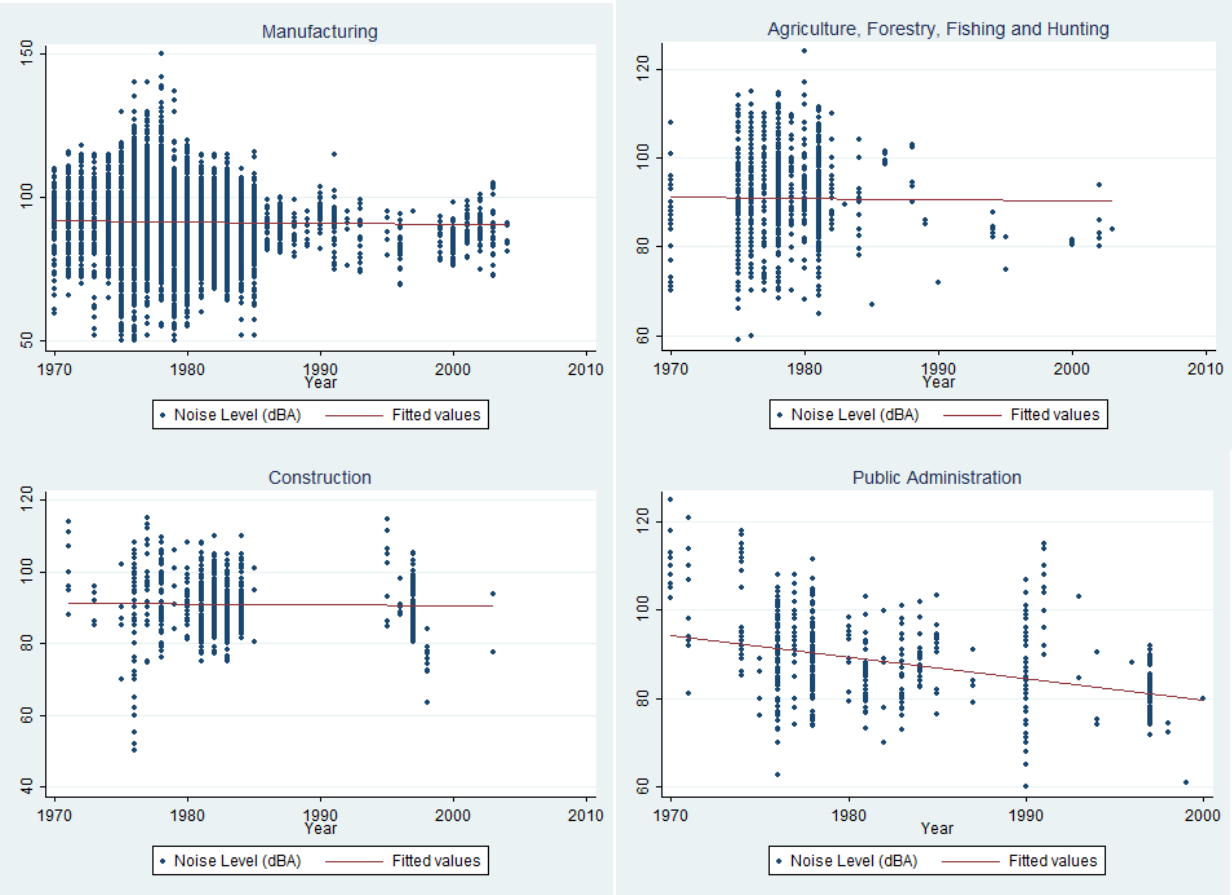


Figure 3. 5 Scatter Plots of Noise Level by Industries

3.1.5 Quality of the Assigned NOC-S Codes

Among the 500 observations selected for the quality assurance assessment, 82% were given the same NOC-S code by both coders. There existed different opinions on the assigned codes in 6% of observations. The divergences were discussed and a more suitable code was selected, and then reassigned to all observations. The rest (12%) were regarded as ambiguous and difficult to decide which assigned code was more appropriate. No change was made to these assigned codes based on the second reviewer's codes.

3.2 National Population Health Survey

3.2.1 Diabetes

3.2.1.1 Characteristics of Cases and Controls

There were 202 diabetes cases reported during follow-up and 1,010 selected controls matched by sex and age. The characteristics of cases and controls are shown in **Table 3. 6**. The distribution of noise exposure groups among cases and controls was quite similar ($p = 0.915$). Compared to controls, cases were more likely to be physically inactive and overweight or obese. There was a higher proportion of cases than controls among regular drinkers. The distribution of categories of smoking status among cases and controls was similar. There was a higher proportion of cases who had hypertension in the first cycle compared to controls. In terms of the socioeconomic status, controls were more likely to have higher education and higher family income compared to cases.

3.2.1.2 Collinearity among Covariates

According to the results from the spearman's correlation, the strongest correlation was found between family income and education ($r = 0.31$). There was no collinearity between the covariates used for model building and all covariates were offered to the multivariable model. (**Table 3. 7**)

3.2.1.3 Association between Noise Exposure and Covariates

Based on the results of the chi-square tests between the noise exposure variable and other covariates, strong associations were found between noise exposure and sex (most men were in the high exposure group while most women were in low or medium exposure group, $p < 0.001$), age (more people aged 50 years and younger were in the high exposure group while more people

aged over 50 years were in the medium exposure group, $p < 0.001$), education (people who had some post-secondary education were more likely to be in the medium exposure group while the people belonging to other education categories were more likely to be in the high exposure group, $p = 0.04$), and family income (people who had lower income tended to have low exposure while those who had higher income had high exposure, $p < 0.001$). The detailed bivariate analysis results between noise exposure and covariates are shown in **Table 3. 8**.

3.2.1.4 Associations between Noise Exposure, Other Covariates and Diabetes

The unadjusted ORs calculated from bivariate analysis between diabetes and all predictors using a simple logistic regression model are listed in **Table 3. 9**. Obese status, lower physical activity, and hypertension were significantly associated with diabetes. Noise exposure, smoking, drinking, income and education were not.

After the predictor selecting process, the final model contained all offered predictors and was used to estimate adjusted ORs. For detailed information on how the final multiple regression model was selected, please see **Appendix B:**, **Table B. 1**. According to the adjusted ORs, no statistically significant association was found between noise exposure and diabetes. In terms of covariates, only obesity was associated with diabetes. The association showed an exposure-response relationship. For physical activity, smoking and hypertension, though no statistically significant results were found, there existed associations between diabetes and these covariates: being physically inactive, a current smoker, and having hypertension were all associated with an increased risk of diabetes. The association between drinking and diabetes was not clear since neither a statistical significance nor a dose-response relationship was found. In terms of socio-economic status, higher SES (better education, higher income) was associated with a lower risk of diabetes (**Table 3. 9**)

Table 3. 6 Characteristics of Diabetes Cases and Controls

	Cases	Percent	Controls	Percent	Chi-square Test
	N = 202	(%)	N = 1010	(%)	
Exposure Groups					
Low-exposure (< 85 dBA-year)	60	29.7	286	28.3	
Medium-exposure (85 – 95 dBA-year)	64	31.7	331	32.8	p = 0.915
High-exposure (>95 dBA-year)	78	38.6	393	38.9	
Sex					
Male	117	57.9	585	57.9	p = 1
Female	85	42.1	425	42.1	
Age					
< 30	19	9.4	95	9.4	
31 – 40	39	19.3	195	19.3	p = 1
41 – 50	94	46.5	470	46.5	
> 50	50	24.8	250	24.8	
Obese					
Underweight / Normal Weight	25	12.4	314	31.1	
Overweight	76	37.6	453	44.9	
Obese I	60	29.7	179	17.7	p < 0.001
Obese II	25	12.4	42	4.1	
Obese III	16	7.9	22	2.2	
Physical Activity					
Active	43	21.3	280	27.7	
Moderate	45	22.3	281	27.8	p = 0.008
Inactive	114	56.4	449	44.5	
Smoke					
Current Smoker	37	18.3	205	20.3	
Former Smoker	111	55.0	515	51.0	p = 0.584
Never Smoked	54	26.7	290	28.7	
Drinking Status					
Regular Drinker	115	56.9	709	70.2	
Former Drinker	36	17.8	121	12.0	p = 0.001
Occasional Drinker / Never Drank	51	25.3	180	17.8	
Hypertension					
Yes	30	14.9	66	6.5	p < 0.001
No	172	85.1	944	94.5	
Education					
Less than Secondary School Graduation	35	17.3	164	16.2	
Secondary School Graduation	34	16.8	120	11.9	p = 0.037
Some Post-secondary	63	31.2	273	27.0	
Post-secondary Graduation	70	34.7	453	44.9	
Family Income					
< $ 40,000	61	30.2	265	26.2	
$ 40,000 - $ 79,999	86	42.6	353	35.0	p = 0.007
> $ 80,000	55	27.2	392	38.8	

Table 3. 7 Correlation Matrix for Covariates

	Age	Sex	Obese	Physical Activity	Smoking Status	Drinking Status	Hypertension	Education	Family Income
Age	1								
Sex	-0.0096	1							
Obese	-0.0341	-0.0872	1						
Physical Activity	-0.0216	0.0422	0.0888	1					
Smoking Status	0.0515	0.1072	0.0619	-0.0664	1				
Drinking Status	0.1018	0.1302	0.1117	0.1332	0.0435	1			
Hypertension	-0.1119	0.0272	-0.1491	-0.1007	-0.0499	-0.1047	1		
Education	-0.1488	0.0524	-0.097	-0.1353	0.127	-0.1367	0.0662	1	
Family Income	-0.2623	-0.1497	-0.0608	-0.1787	0.0713	-0.3044	0.1073	0.3081	1

Table 3. 8 Associations between Exposure Groups and Covariates

	Exposure Group						Chi-square
	Low	%	Medium	%	High	%	Test
Sex							
Male	128	37.0	194	49.1	380	80.7	p < 0.001
Female	218	63.0	201	50.9	91	19.3	
Age							
< 30	29	8.4	50	12.7	35	7.4	
31 – 40	50	14.5	75	19.0	109	23.1	p < 0.001
41 – 50	159	46.0	175	44.3	230	48.8	
> 50	108	31.1	95	24.0	97	20.7	
Obese							
Underweight / Normal Weight	109	31.5	114	28.9	116	24.6	
Overweight	133	38.4	174	44.1	222	47.1	p = 0.108
Obese	104	30.1	107	27.0	133	28.3	
Physical Activity							
Active	100	28.9	100	25.3	124	26.3	
Moderate	91	26.3	113	28.6	131	27.8	p = 0.849
Inactive	155	44.8	182	46.1	216	45.9	
Smoke							
Current Smoker	57	16.5	86	21.8	99	21.0	
Former Smoker	176	50.9	199	50.4	251	53.3	p = 0.141
Never Smoked	113	32.6	110	27.8	121	25.7	
Drinking Status							
Regular Drinker	216	62.4	272	68.9	336	71.3	
Former Drinker	54	15.6	45	11.4	58	12.3	p = 0.071
Occasional Drinker / Never Drank	76	22.0	78	19.7	77	16.4	
Hypertension							
Yes	35	10.1	24	6.1	37	7.9	p = 0.127
No	311	89.9	371	93.9	434	92.1	
Education							
Less than Secondary School	52	15.0	55	13.9	92	19.5	
Graduation							
Secondary School Graduation	42	12.1	49	12.4	63	13.4	p = 0.040
Some Post-secondary	104	30.1	126	31.9	106	22.5	
Post-secondary Graduation	148	42.8	165	41.8	210	44.6	
Family Income							
< $ 40,000	117	33.8	121	30.6	88	18.7	
$ 40,000 - $ 79,999	118	34.1	138	34.9	183	38.9	p < 0.001
> $ 80,000	111	32.1	136	34.5	200	42.4	

Table 3. 9 Summary of Results for Diabetes from Single Logistic Regression and the Final Multivariate Logistic Regression

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Exposure		
Low-exposure (< 85 dBA-year)	1	1
Medium-exposure (85 – 95 dBA-year)	0.92 (0.62 – 1.36)	0.93 (0.61 - 1.41)
High-exposure (>95 dBA-year)	0.94 (0.63 – 1.40)	1.04 (0.67 - 1.59)
Obese Status		
Underweight / Normal Weight	1	1
Overweight	2.06 (1.27 – 3.34)	2.14 (1.31 - 3.51)
Obese I	4.22 (2.53 – 7.01)	4.03 (2.39 - 6.80)
Obese II	7.72 (4.02 – 14.8)	6.88 (3.47 - 13.7)
Obese III	9.46 (4.39 – 20.4)	7.40 (3.26 - 16.8)
Physical Activity		
Active	1	1
Moderate	1.01 (0.65 – 1.58)	0.93 (0.58 - 1.49)
Inactive	1.73 (1.17 – 2.54)	1.37 (0.91 - 2.06)
Smoke		
Never Smoked	1	1
Former Smoker	1.16 (0.81 – 1.66)	1.09 (0.74 - 1.59)
Current Smoker	0.97 (0.62 – 1.52)	1.22 (0.75 - 1.99)
Drinking Status		
Occasional Drinker / Never Drank	1	1
Former Drinker	1.01 (0.62 - 1.65)	1.01 (0.60 - 1.71)
Regular Drinker	0.55 (0.38 - 0.81)	0.74 (0.48 - 1.14)
Hypertension at Cycle 1		
No	1	1
Yes	2.67 (1.64 – 4.34)	1.62 (0.94 - 2.78)
Education		
Less than Secondary School Graduation	1	1
Secondary School Graduation	1.32 (0.78 – 2.26)	1.60 (0.90 - 2.84)
Some Post-secondary	1.09 (0.68 – 1.72)	1.37 (0.84 - 2.25)
Post-secondary Graduation	0.71 (0.45 – 1.12)	1.05 (0.64 - 1.72)
Family Income		
< $40,000	1	1
$ 40,000 - $ 79,999	1.02 (0.70 – 1.48)	1.21 (0.80 - 1.84)
> $ 80,000	0.57 (0.37 – 0.87)	0.86 (0.53 - 1.39)

3.2.2 Rheumatoid Arthritis

3.2.2.1 Characteristics of Cases and Controls

There were 91 reported rheumatoid arthritis cases during follow-up and 455 controls matched by sex and age. The characteristics of cases and controls are shown in **Table 3. 10**. There was little difference in noise exposure between cases and controls ($p = 0.974$). Controls were more likely to have higher education and family income compared to cases. In terms of the obese status, physical activity, and smoking status, the distribution of cases and controls among different categories was relatively similar.

3.2.2.2 Collinearity among Covariates

The correlation matrix for covariates is shown in **Table 3. 11**. The strongest correlation was found between education and family income ($r = 0.24$). There was no significant collinearity found between any of the two covariates that would influence the validity of the regression model and all covariates were offered to the multivariable model.

3.2.2.3 Association between Noise Exposure and Covariates

Similar to the diabetes sub-cohort, strong associations were found between noise exposure and sex (most men were in the high exposure group while most women were in low or medium exposure group, $p < 0.001$), age (people aged between 35 and 44 years were more likely to have high exposure while those not belonging to this age range tended to have medium exposure, $p = 0.016$), obesity (people who were overweight or obese were more likely to have high exposure while those who had normal weight or were underweight were more likely to have the medium exposure, $p = 0.043$), and education (people who had less education tended to have high exposure while people who had more education tended to be in the low or medium exposure group, $p = 0.021$). The detailed bivariate analyses between noise exposure and covariates are

shown in **Table 3. 12**.

3.2.2.4 Association between Noise Exposure and Rheumatoid Arthritis

Unadjusted ORs estimated from bivariate analyses between rheumatoid arthritis variable and all predictors using a simple logistic regression model are listed in **Table 3. 13**. Only family income had a significant association with rheumatoid arthritis.

After the predictor selection process, the final model contained all offered predictors and was used to estimate adjusted ORs. For detailed information on how the final multiple regression model was selected, please find in **Appendix B:**, **Table B. 2**. In the multiple logistic regression model, there was no statistically significant association between noise exposure and rheumatoid arthritis. In terms of covariates, people who were current smokers or had some post-secondary education were at higher risk of rheumatoid arthritis, while moderate physical activity or higher family income were associated with a lower risk of rheumatoid arthritis. The association between obesity and RA was not statistically significant. (**Table 3. 13**)

Table 3. 10 Characteristics of Rheumatoid Arthritis Cases and Controls

	Cases	Percent	Controls	Percent	Chi-square Test
	N = 91	(%)	N = 455	(%)	
Exposure Groups					
Low-exposure (< 85 dBA-year)	25	27.5	120	26.4	
Medium-exposure (85 – 95 dBA-year)	34	37.4	171	37.6	p = 0.974
High-exposure (>95 dBA-year)	32	35.1	164	36.0	
Sex					
Male	43	47.3	215	47.3	p = 1
Female	48	52.7	240	52.7	
Age					
< 35	29	31.9	145	31.9	
35 – 44	33	36.3	165	36.3	p = 1
>= 45	29	31.8	145	31.8	
Obese					
Underweight or Normal Weight	32	35.2	168	36.9	
Overweight	37	40.6	180	39.6	p = 0.951
Obese	22	24.2	107	23.5	
Physical Activity					
Active	26	28.6	107	23.5	
Moderate	19	20.9	139	30.6	p = 0.166
Inactive	46	50.5	209	45.9	
Smoke					
Current Smoker	23	25.3	84	18.5	
Former Smoker	44	48.3	228	50.1	p = 0.290
Never Smoked	24	26.4	143	31.4	
Education					
Secondary School Graduation or Less	25	27.5	125	27.5	
Some Post-secondary	34	37.4	115	25.3	p = 0.039
Post-secondary Graduation	32	35.1	215	47.2	
Family Income					
< $ 40,000	24	26.4	90	19.8	
$ 40,000 - $ 79,999	39	42.8	158	34.7	p = 0.034
> $ 80,000	28	30.8	207	45.5	

Table 3. 11 Correlation Matrix for Covariates

	Age	Sex	Obese	Physical Activity	Smoking Status	Education	Family Income
Age	1						
Sex	-0.1379	1					
Obese	0.1274	-0.2093	1				
Physical Activity	-0.0049	-0.0213	0.1637	1			
Smoking Status	0.131	0.0845	0.0096	-0.041	1		
Education	-0.1405	0.0686	-0.0435	-0.0236	0.1229	1	
Family Income	-0.1773	-0.0985	-0.0737	-0.1222	0.0857	0.2403	1

Table 3. 12 Associations between Exposure Groups and Covariates

	Exposure Group						Chi-square
	Low	%	Medium	%	High	%	Test
Sex							
Male	44	30.3	70	34.1	144	73.5	p < 0.001
Female	101	69.7	135	65.9	52	26.5	
Age							
< 35	41	28.3	79	38.5	54	27.6	
35 – 44	49	33.8	63	30.7	86	43.9	p = 0.016
>= 45	55	37.9	63	30.8	56	28.5	
Obese							
Underweight or Normal Weight	58	40.0	82	40.0	60	30.6	
Overweight	46	31.7	84	41.0	87	44.4	p = 0.043
Obese	41	28.3	39	19.0	49	25.0	
Physical Activity							
Active	36	24.8	46	22.4	51	26.0	
Moderate	39	26.9	60	29.3	59	30.1	p = 0.848
Inactive	70	48.3	99	48.3	86	43.9	
Smoke							
Current Smoker	24	16.6	41	20.0	42	21.4	
Former Smoker	77	53.1	97	47.3	98	50.0	p = 0.705
Never Smoked	44	30.3	67	32.7	56	28.6	
Education							
Secondary School Graduation or Less	43	29.7	47	22.9	60	30.6	p = 0.021
Some Post-secondary	50	34.5	57	27.8	42	21.4	
Post-secondary Graduation	52	35.8	101	49.3	94	48.0	
Family Income							
< $ 40,000	36	24.8	50	24.4	28	14.3	
$ 40,000 - $ 79,999	53	36.6	72	35.1	72	36.7	p = 0.060
> $ 80,000	56	38.6	83	40.5	96	49.0	

Table 3. 13 Summary of Results for Rheumatoid Arthritis from Single Logistic Regression and the Final Multivariate Logistic Regression

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Exposure		
Low-exposure (< 85 dBA-year)	1	1
Medium-exposure (85 – 95 dBA-year)	0.95 (0.54 – 1.68)	1.01 (0.56 - 1.82)
High-exposure (>95 dBA-year)	0.93 (0.51 – 1.70)	1.07 (0.57 - 2.01)
Obese Status		
Underweight / Normal Weight	1	1
Overweight	1.09 (0.63 – 1.86)	1.09 (0.63 - 1.90)
Obese	1.08 (0.60 - 1.96)	1.11 (0.59 - 2.08)
Physical Activity		
Active	1	1
Moderate	0.57 (0.30 - 1.08)	0.48 (0.25 - 0.93)
Inactive	0.91 (0.54 - 1.52)	0.76 (0.44 - 1.32)
Smoke		
Never Smoked	1	1
Former Smoker	1.67 (0.87 - 3.21)	1.00 (0.56 - 1.78)
Current Smoker	1.17 (0.67 - 2.01)	1.48 (0.75 - 2.94)
Education		
Secondary School Graduation or Less	1	1
Some Post-secondary	1.53 (0.84 - 2.77)	1.86 (1.01 - 3.44)
Post-secondary Graduation	0.74 (0.41 - 1.31)	0.91 (0.50 - 1.66)
Family Income		
< $40,000	1	1
$ 40,000 - $ 79,999	0.90 (0.49 - 1.62)	0.98 (0.53 - 1.80)
> $ 80,000	0.48 (0.26 - 0.90)	0.50 (0.26 - 0.96)

3.2.3 Cardiovascular Disease

3.2.3.1 Characteristics of Cases and Controls

There were 221 reported cardiovascular disease cases during follow-up and 1,105 controls matched by sex and age. The characteristics of cases and controls are shown in **Table 3. 14**. Although the proportion of controls belonging to the high noise exposure group was higher compared to that of cases, the difference was very slight. Compared to controls, cases were more likely to be physically inactive and overweight or obese. The proportion of cases who were current or former smoker was higher compared to that of controls. A higher proportion of cases than controls belonged to the "occasional drinker / never drank" category. Cases were more likely to have hypertension in the first cycle compared to controls. Controls were more likely to have higher education and family income compared to cases.

3.2.3.2 Collinearity among Covariates

The results of correlations between covariates are listed in **Table 3. 15**. The strongest correlation was found between education and family income ($r = 0.36$). There was no significant collinearity found between any of the two covariates that would influence the validity of the regression model and all covariates were offered to the multivariable model.

3.2.3.3 Association between Noise Exposure and Covariates

Based on the results of the chi-square tests between the noise exposure group variable and other covariates, strong associations were found between noise exposure and sex (most men were in the high exposure group while most women were in low or medium exposure group, $p < 0.001$), age (more people aged younger than 50 were in the high exposure group while more people aged elder than 50 were in the low exposure group, $p < 0.001$), smoking status (more people who were current/former smoker were in the high exposure group while more people who never smoked

were in the low exposure group, $p = 0.010$), drinking status (people who drank were more likely to be in the high exposure group while those who seldom drank were more likely to be in the low exposure group, $p < 0.001$), and family income (people who had lower income tended to have low exposure while those who had higher income had high exposure, $p < 0.001$). The detailed bivariate analysis between noise exposure and covariates are shown in **Table 3. 16**.

3.2.3.4 Association between Noise Exposure and Cardiovascular Disease

The results of the bivariate analysis between the CVD and model predictors are shown as unadjusted ORs in **Table 3. 17**. Smoking status drinking status, hypertension, and family income were found to be significantly associated with CVD.

After the predictor selection process, the final model contained all offered predictors and was used to estimate adjusted ORs. For detailed information on how the final multiple regression model was selected, please find in **Appendix B:**, **Table B. 3**. The calculated adjusted ORs from the multiple logistic regression model showed no statistically significant association between noise exposure and CVD (**Table 3. 17**). In terms of covariates, people who used to smoke or had hypertension were at higher risk of CVD. Being a regular drinker or having relatively higher family income was associated with reduced risk of CVD. Although no statistically significant association was found between CVD and obesity, a mild dose-response relationship was observed.

Table 3. 14 Characteristics of CVD Cases and Controls

	Cases	Percent	Controls	Percent	Chi-square Test
	N = 221	(%)	N = 1105	(%)	
Exposure Groups					
Low-exposure (< 85 dBA-year)	76	34.4	339	30.7	
Medium-exposure (85 – 95 dBA-year)	69	31.2	347	31.4	p = 0.490
High-exposure (>95 dBA-year)	76	34.4	419	37.9	
Sex					
Male	115	52.0	575	52.0	p = 1
Female	106	48.0	530	48.0	
Age					
< 30	20	9.1	100	9.1	
31 – 40	52	23.5	260	23.5	p = 1
41 – 50	88	39.8	440	39.8	
> 50	61	27.6	305	27.6	
Obese					
Underweight / Normal Weight	58	26.3	329	29.8	
Overweight	94	42.5	495	44.8	p = 0.188
Obese	69	31.2	281	25.4	
Physical Activity					
Active	52	23.5	243	22.0	
Moderate	54	24.4	351	31.8	p = 0.093
Inactive	115	52.1	511	46.2	
Smoke					
Current Smoker	41	18.6	215	19.5	
Former Smoker	137	62.0	574	52.1	p = 0.011
Never Smoked	43	19.4	314	28.4	
Drinking Status					
Regular Drinker	126	57.0	744	67.3	
Former Drinker	39	17.7	141	12.8	p = 0.012
Occasional Drinker / Never Drank	56	25.3	220	19.9	
Hypertension					
Yes	30	13.6	60	5.4	p < 0.001
No	191	86.4	1045	94.6	
Education					
Less than Secondary School	40	18.1	160	14.5	
Graduation					
Secondary School Graduation	29	13.1	145	13.1	p = 0.215
Some Post-secondary	68	30.8	302	27.3	
Post-secondary Graduation	84	38.0	498	45.1	
Family Income					
< $ 40,000	72	32.6	277	25.1	
$ 40,000 - $ 79,999	89	40.3	372	33.7	p < 0.001
> $ 800,000	60	27.1	456	41.2	

Table 3. 15 Correlation Matrix for Covariates

	Age	Sex	Obese	Physical Activity	Smoking Status	Drinking Status	Hypertension	Education	Family Income
Age	1								
Sex	-0.0349	1							
Obese	-0.0105	-0.1316	1						
Physical Activity	-0.0547	0.0032	0.13	1					
Smoking Status	0.1444	0.1036	0.0355	-0.0755	1				
Drinking Status	0.0923	0.1692	0.0309	0.0914	0.0992	1			
Hypertension	-0.0987	-0.017	-0.0857	-0.0112	-0.0137	-0.0106	1		
Education	-0.1757	0.0067	-0.0351	-0.1223	0.1133	-0.1269	0.0155	1	
Family Income	-0.2954	-0.1645	-0.0172	-0.1054	0.0472	-0.2374	0.0445	0.3561	1

Table 3. 16 Associations between Exposure Groups and Covariates

	Exposure Groups						Chi-square Test
	Low	%	Medium	%	High	%	
Sex							
Male	132	31.8	177	42.5	381	77.0	p < 0.001
Female	283	68.2	239	57.5	114	23.0	
Age							
< 30	34	8.2	44	10.6	42	8.5	
31 – 40	92	22.2	95	22.8	125	25.3	p < 0.001
41 – 50	136	32.8	164	39.4	228	46.1	
> 50	153	36.8	113	27.2	100	20.1	
Obese							
Underweight / Normal Weight	132	31.8	125	30.0	130	26.3	
Overweight	183	44.1	170	40.9	236	47.7	p = 0.141
Obese	100	24.1	121	29.1	129	26.0	
Physical Activity							
Active	89	21.4	90	21.6	116	23.4	
Moderate	130	31.3	127	30.5	148	29.9	p = 0.949
Inactive	196	47.3	199	47.9	231	46.7	
Smoke							
Current Smoker	61	14.7	82	19.7	113	22.8	
Former Smoker	225	54.2	219	52.6	267	53.9	p = 0.010
Never Smoked	129	31.1	115	27.7	115	23.3	
Drinking Status							
Regular Drinker	237	57.1	276	66.3	357	72.1	
Former Drinker	64	15.4	49	11.8	67	13.5	p < 0.001
Occasional Drinker / Never	114	27.5	91	21.9	71	14.3	
Drank							
Hypertension							
Yes	34	8.2	29	7.0	27	5.5	p = 0.258
No	381	91.8	387	93.0	468	94.5	
Education							
Less than Secondary School	63	15.2	55	13.2	82	16.6	
Graduation							
Secondary School Graduation	63	15.2	48	11.5	63	12.7	p = 0.442
Some Post-secondary	119	28.6	119	28.6	132	26.7	
Post-secondary Graduation	170	41.0	194	46.7	218	44.0	
Family Income							
< $ 40,000	138	33.3	123	29.6	88	17.8	
$ 40,000 - $ 79,999	138	33.3	144	34.6	179	36.2	p < 0.001
> $ 800,000	139	33.6	149	35.8	228	46.0	

Table 3. 17 Summary of Results for Cardiovascular Disease from Single Logistic Regression and the Final Multivariate Logistic Regression

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Exposure		
Low-exposure (< 85 dBA-year)	1	1
Medium-exposure (85 – 95 dBA-year)	0.87 (0.61 – 1.26)	0.87 (0.59 - 1.28)
High-exposure (>95 dBA-year)	0.77 (0.53 – 1.14)	0.85 (0.57 - 1.27)
Obesity Status		
Underweight / Normal Weight	1	1
Overweight	1.08 (0.75 - 1.55)	1.12 (0.77 - 1.63)
Obese	1.39 (0.95 - 2.04)	1.18 (0.79 - 1.78)
Physical Activity		
Active	1	1
Moderate	0.71 (0.47 – 1.08)	0.65 (0.42 - 1.01)
Inactive	1.05 (0.73 – 1.50)	0.91 (0.62 - 1.34)
Smoke		
Never Smoked	1	1
Former Smoker	1.76 (1.21 – 2.56)	1.81 (1.23 - 2.67)
Current Smoker	1.40 (0.87 – 2.24)	1.30 (0.80 - 2.13)
Drinking Status		
Occasional / Never Drank	1	1
Former Drinker	1.08 (0.69 - 1.70)	1.03 (0.64 - 1.65)
Regular Drinker	0.64 (0.45 - 0.92)	0.68 (0.46 - 1.00)
Hypertension at Cycle 1		
No	1	1
Yes	2.73 (1.71 – 4.36)	2.86 (1.74 - 4.69)
Education		
Less than Secondary School Graduation	1	1
Secondary School Graduation	0.80 (0.47 – 1.34)	1.00 (0.59 - 1.71)
Some Post-secondary	0.89 (0.57 – 1.40)	1.12 (0.70 - 1.80)
Post-secondary Graduation	0.67 (0.44 – 1.02)	0.96 (0.60 - 1.52)
Family Income		
< $40,000	1	1
$ 40,000 - $ 79,999	0.87 (0.61 – 1.24)	0.95 (0.65 - 1.39)
> $ 80,000	0.46 (0.31 – 0.68)	0.52 (0.34 - 0.81)

Chapter 4: Discussion

4.1 Summary of Key Findings

4.1.1 Diabetes

No association was observed between occupational noise exposure and diabetes in the present study. The unadjusted ORs for diabetes associated with medium and high noise exposure groups were 0.92 (95% CI: 0.62 – 1.36) and 0.94 (95% CI: 0.63 – 1.40) respectively. After adjusting for other covariates, the direction of the OR for high exposure group changed (1.04, 95% CI: 0.67 – 1.59), but the magnitude of change was quite small and the OR was not statistically significant.

A review of the literature indicated that there has been only one study of the direct association between noise exposure and diabetes, and that was a broader environmental study. Sorensen *et al*. (2012) investigated long-term exposure to residential road traffic noise and incidence of diabetes in a large cohort study. They found incidence risk ratios of 1.11 (95% CI: 1.03 – 1.19) and 1.14 (95% CI: 1.06 – 1.22) per 10-dB increase in road traffic noise at diagnosis and during the 5 years preceding diagnosis, respectively. The associations were slightly stronger when using a longer period of exposure (5 years) compared to shorter period of exposure (1 year). Although this study provided some support to a direct association between noise and diabetes, the results may not be generalized to occupational noise since environmental noise may work by a different mechanism in which the stress response may not dominate. Sorensen *et al*. proposed that the sleep disturbances (e.g. short sleep duration, reduced sleep quality, changes in sleep stages) resulting from night-time exposure to traffic noise might be a possible intermediate stage which led to the diabetes outcome.

There are however studies demonstrating a positive association between stress and diabetes (Djindjic *et al*., 2012; Li *et al*., 2012; Novak *et al*., 2012). Djindjic *et al*. and Li *et al*. studied work-related stress and Novak et al. studied the stress from various aspects of life (both at work

and at home). However, the measured stress in these studies was not a surrogate of noise exposure; their results provided support for the second part of the proposed biological model, the stress-disease relationship. The perception of noise (i.e. the noise-stress response) is a complex process in which two major pathways (direct and indirect) interact in a very complicated way and many other parameters are involved (e.g. noise level, personal susceptibility, attitude towards noise) which were not addressed in these studies. Although they did not examine the direct association between noise and diabetes, they did provide some ideas to explain the negative results of our study. Since the stress – diabetes association was supported by these studies and a noise – stress response has been demonstrated in previous studies, it would be expected that there is a positive association between noise exposure and diabetes, yet we did not find this in our study. Assuming then that there is a true relationship, why might our study have not seen it? It is possible that the noise in our study was not stressful enough (high enough or of sufficient duration or both) to trigger the stress response (i.e. noise exposure was not cumulated sufficiently due to limited time period to estimate exposure duration.). It is also possible that some biases (e.g. exposure misclassification) in the study may dilute the association. Given the relatively well-studied association between occupational noise exposure and CVD, we used CVD in this study as a sensitivity test to examine that the validity of the methods of this study. Since no association was found between occupational noise exposure and CVD in the subjects of NPHS, this supports the idea that biases in the study diluted the estimated association. The biases that may influence the validity of the methods and their sources are discussed in following sections.

Subjects' obesity status was strongly associated with diabetes and a clear trend was found where the more severe the obesity, the higher the risk of diabetes (overweight: 2.14, obese I: 4.03, obese II: 6.88, obese III: 7.40). Being physically inactive increased the risk of diabetes (1.37, 95% CI: 0.91 – 2.06) though the positive association was not statistically significant. Hypertension was also positively associated with diabetes (1.62, 95% CI: 0.94 – 2.78). These associations were consistent with the risk factors described elsewhere for diabetes (Canadian Diabetes Association, 2013), which means that the measurement of the diabetes outcome and these covariates were relatively reliable.

4.1.2 Rheumatoid Arthritis

Our results indicate that there was no observed association between occupational noise exposure and RA in the current study. The unadjusted ORs for RA associated with the medium and high noise exposure groups showed decreased but non-statistically significant association between occupational noise exposure and RA (medium exposure group: 0.95, 95% CI: 0.54 – 1.68; high exposure group: 0.93, 95% CI: 0.51 – 1.70). After adjusting for other covariates, the direction of the association changed but the association was weak and remained non-statistically significant (medium exposure group: 1.01, 95% CI: 0.56 – 1.82; high exposure group: 1.07, 95% CI: 0.57 – 2.01). The change of direction occurred when adding the education and family income covariates, indicating that they might be confounders.

A literature review found no previous studies that focused on the association between noise and RA for comparison, though findings of an unpublished recent environmental noise study that studied RA was also negative (personal communication with Hugh Davies). Our negative findings may reflect a true lack of association between noise and RA, or might result from biases in the study; these are discussed in later sections.

Looking at other risk factors, compared to the high activity group, having moderate physical activity was associated with a decreased risk of RA (0.48, 95% CI: 0.25 – 0.93); this is consistent with our speculation that some benefits of moderate physically activity but more extreme levels causing more damage to a joint. Current smokers were at higher risk of RA though the OR was not statistically significant (1.48, 95% CI: 0.75 – 2.94). This is consistent with previous relevant information on RA (Centers for Disease Control and Prevention, 2012; Statistics Canada, 2006). Having higher family income was associated with a decreased risk (0.50, 95% CI: 0.26 – 0.96). This is also consistent with a previous study that used the first cycle of the NPHS in a cross-sectional analysis (Wang *et al.*, 2000).

4.1.3 Cardiovascular Disease as "Sensitivity Analysis"

The ORs for CVD in medium and high noise exposure groups were 0.87 (95% CI: 0.61 – 1.26) and 0.77 (95% CI: 0.53 – 1.14) respectively. After adjusting for other covariates, the direction of the ORs remained the same and the magnitude of the ORs only changed slightly (medium exposure group: 0.87, 95% CI: 0.59 – 1.28; high exposure group: 0.85, 95% CI: 0.57 – 1.27). The results indicated a decreased risk of heart disease associated with occupational noise exposure although the association was not statistically significant, that is opposite to the direction hypothesized.

The association between noise exposure and CVD has been studied for decades and, as relevant research methodologies became more and more sophisticated, a positive association has gradually been accepted even though negative studies have still occurred in recent years (Suadicani *et al*., 2012). Most studies focusing on the noise-CVD association were conducted within two major domains: occupational noise and environmental noise. Although many previous studies focusing on environmental noise have found positive association between noise and CVD (Eriksson *et al*., 2010; Babisch and van Kamp, 2009; Kluizenaar *et al*., 2007; Babisch *et al*., 2005), they are not discussed further here because environmental noise likely works by a different mechanism.

In Virkkunen *et al.* (2005), exposure to occupational noise was associated with a moderate but statistically significant increase in coronary heart disease risk among workers that persisted even after they retired. McNamee *et al.* (2006) found increases in the risk of ischemic heart disease in one of two studied industrial plants; the negative result in the second plant was attributed to poor exposure assessment and subsequent misclassification. Gan *et al*. (2011) studied the noise and CVD association in the general population of the USA and found an increased risk of angina pectoris (OR = 2.91, 95% CI: 1.35 – 6.26), coronary heart disease (OR = 2.04, 95% CI: 1.16 – 3.58), and isolated diastolic hypertension (OR = 2.23, 95% CI: 1.21 – 4.12). Lee *et al*. (2009) studied 530 workers at a metal manufacturing factory in Korea and observed an increase of systolic blood pressure in all three noise exposed groups. In British Columbia, a retrospective

cohort study of lumber mill workers found that long-term exposure to occupational noise was associated with an increased risk of acute myocardial infarction death (Davies *et al.*, 2005). In another examination of the same BC sawmill workers, a positive association between noise exposure above 85 dBA and hypertension was found (Sbihi *et al*., 2008). In a meta-analysis based on 15 papers from 1950 to 2008, a statistically significant increase in systolic and diastolic blood pressure was found in workers in the high exposure group. In this exposure group, the prevalence of hypertension and ECG abnormalities were also higher (Tomei *et al*., 2010).

In our study, being overweight (OR: 1.12, 95% CI: 0.59 – 1.28) and obese (OR: 1.18, 95% CI: 0.79 – 1.78) were associated with an increased risk of CVD, though the associations were not statistically significant. People who smoked were at higher risk and the positive association was more obvious in former smokers (OR: 1.81, 95% CI: 1.23 – 2.67) than current smokers (OR: 1.30, 95% CI: 0.80 – 2.13). Having hypertension was significantly associated with increased risk of CVD (OR: 2.86, 95% CI 1.74 – 4.69). All these factors (obesity, smoking, and hypertension) are known risk factors for CVD (WHO, 2012). The consistency between our results and those of prior studies indicates that the significant bias in the measurement of CVD and the covariates was unlikely; thus if there is a true relation between noise and CVD as evidenced by earlier studies, the most likely source of bias that might obscure the relation in our study is from the exposure assessment.

4.2 Potential Impact of Bias

In the current study, there were potential biases that could have influenced the exposure assessment as well as the measurement of health outcome and covariates, and which may have had further impact on the validity of the results. The major biases and their effect on the study results are discussed in this section.

4.2.1 Misclassification in Health Outcome and Covariates

The measurement of health outcome was based on self-reported diagnosis by a health professional. Therefore, the accuracy of the reported information determined the degree of misclassification in the health outcomes. It is true that information provided by some subjects on the same question varied among different cycles (e.g. one reported CVD in the first cycle, then became non-CVD in the second and third cycles, finally had CVD in the forth cycle), which indicated some quality issues about the reported information. In subjects who reported disease status, it is thought that the severe cases may remember relevant information about their disease (e.g. diagnosis time) and provide more reliable information compared to those who only had mild symptoms (Coughlin, 1990). On the other hand, not reporting a health outcome did not ensure that the subject was disease free; for example, people might be at the early stage of the disease or their disease symptoms were not obvious enough to draw their attention to seek a health professional's advice. Baker *et al*. (2011) used the Ontario Health Insurance Plan (OHIP) as a relatively reliable 'gold standard' and compared the medical record in its system to the health status reported by the NPHS subjects in the province of Ontario. They found correlation coefficients of 0.71 and 0.17 between OHIP records and self-reported health status in NPHS for diabetes and arthritis respectively. After quantifying the measurement error, the ratios of the error variance to the total variance were 0.35 and 0.88 for diabetes and arthritis respectively. When decomposing the error variance, for diabetes, the large proportion of variance came from false negatives (72%) while more error variance was due to false positives for arthritis (93%). In the thirteen health conditions (heart disease was not studied) Baker studied, diabetes had the smallest ratio of the error variance to the total variance while that for arthritis was the second largest. This study revealed some problems with the validity of self-reported health status in the NPHS. The direction and magnitude of the misclassification in health outcome measurement was largely determined by the ratio of false negatives to false positives and the distribution of these false negatives and false positives among different exposure groups. Therefore, without knowing how the false negatives and false positives distributed among different exposure groups, the effect of misclassification in measurement of health outcomes on the regression estimates was difficult to assess. For diabetes, if we assumed the misclassification was non-differential among exposure

groups, the ORs of the current study were likely overestimated. But the estimates in the study were very close to 1. So it was more likely that the biases in exposure assessment were more of a problem responsible for these negative results. In terms of RA, because the arthritis studied in Baker *et al*.'s study included all types of arthritis (osteoarthritis, rheumatoid, and other) and RA constituted a small proportion of the total, the misclassification in measurement of RA becomes more complex and hard to evaluate. As for CVD, although it was not studied in Baker *et al*.'s study, we might assume a major source of error from false negatives and a similar effect of misclassification on the estimates.

Another source of misclassification in the measurement of diabetes might come from the failure to exclude other diabetes types, especially type-1 diabetes. Ng *et al*. (2008) developed an algorithm to differentiate diabetes types in the Canadian Community Health Survey and it was adapted and modified in Dinca-Panaitescu *et al*.'s study (2012) to the NPHS longitudinal data to distinguish type-2 diabetes from other types of diabetes. In their study, the type-1 diabetes cases were excluded if they were younger than 30 at interview and started using insulin within 6 month of diagnosis. In the current study, although some type-1 diabetes cases might be excluded because of the inclusion criterion of aged between 18 and 55, others were inevitably retained in the sub-cohort and misclassified as type-2 diabetes. However, given the small proportion (2%) of type-1 diabetes (n = 27) in total diabetes cases (n = 1340) indicated in Dinca-Panaitescu *et al*.'s study, the impact of this misclassification was likely mild.

In terms of covariates, all the covariates were treated as time-stable even though some of them could be time-varying. In order to assure the most up-to-date data was obtained, the information on these covariates was from the latest cycle before the end of follow-up period. Some missing values were filled by obtaining information from earlier cycles. For these reasons, as well as others, some misclassification in the measurement of covariates was inevitable. However in the multivariable models, the associations between the health outcomes and covariates were consistent with current knowledge and therefore, the impact of misclassification on the internal associations between outcomes and covariates was assumed to be mild.

4.2.2 Biases in Exposure Assessment

If the influence from misclassification in health outcome and covariates on the regression estimates was mild, then those biases associated with exposure assessment could be the major reason resulting in the negative results. The exposure assessment part is always a challenging part in occupational epidemiological studies. Generally, the exposure assessment method of the current study can be broken into five stages: sampling, coding, building the JEM, linking two datasets, and estimating CNE. Biases and errors that could occur each of these stages are discussed in following section.

4.2.2.1 Sampling Stage

A potentially substantial source of bias in this stage was related to the sampling devices used to collected noise measurements. The noise samples in WorkSafeBC's noise exposure dataset were collected either by sound level meter or dosimeter. To estimate the cumulative noise exposure for each subject in the NPHS, noise exposure level at individual level based on the subject's NOC-S and/or NAICS codes was required. Therefore, personal sample was preferable to area or "grab" sample. The dosimeter is expected to yield a more accurate estimation of personal exposure because the dosimeter is attached to the subject being sampled and it takes into account the different tasks performed by the subject and the variability of noise exposure (CCOHS, 2004). Accurate noise levels for occupation and/or industry are required to estimate the cumulative noise exposure for each individual in NPHS and reduce exposure misclassification. Therefore, personal exposure is preferable in this study but the majority of samples (62 %) were collected using a sound level meter. Overall, there was only a 0.2 dBA difference between the mean levels of the two sampling type (statistically significant, but the n was very large).

However, when comparing the difference between the two sampling methods within occupations, the sound level meter tended to underestimate the noise level in some occupational groups at the 1-digit NOC-S level and the situation was more varied when more specific occupations (3-digit or 4-digit NOC-S level) were considered and the situation was similar when comparing the two

sampling methods in different industries. Therefore, it is difficult to conclude how the different sampling methods influenced the results but it appears likely that the use of sampling type was randomly distributed and thus resulting misclassification is non-differential.

4.2.2.2 Coding Stage

Each collected samples was assigned a CU code and then aggregated into WorkSafeBC's original noise exposure dataset. These CU codes were then transcribed into 4-digit NAICS codes based on a CU – NAICS codes "cross-walk" that was created by other UBC researchers and has been evolved and refined through use in several other studies of WorkSafeBC data (personal communication with Lillian Tamburic).

In terms of occupation codes, the assignment of NOC-S codes was conducted based mainly on the job description variable, from which a corresponding 4-digit NOC-S code was assigned. Two strategies were applied to reduce error and assure the quality of the assigned NOC-S codes: (1) only measurements that had the highest level of confidence (on a 3-part scale) for assigned NOC-S code were retained in the dataset for JEM building (90% of original dataset); and (2) after the code assigning process, a fraction of the measurements were duplicate coded by a second hygienist independently and these codes were compared with those assigned in the first round. The comparison showed a relatively high consistency (82% of the 500 selected measurements). Moreover, when divergence was found, the more appropriate code was selected and replaced all the incorrect ones in the dataset, which also reduce the error in the assigned NOC-S codes.

4.2.2.3 JEM Building Stage

The building of the JEM was conducted by calculating the mean noise levels for the NOC-S and NAICS codes at four digit and two digit level. Considering that the noise exposure for the same occupation (i.e. same NOC-S) in different industries (i.e. different NAICS) could be different, the mean noise levels were also calculated for each combination of 4-digit NOC-S and 4-digit

NAICS, but only if the number of measurements for that NOC-S NAICS pair was larger than ten. The JEM provided noise levels for subjects in the NPHS and therefore its quality had significant impact on the final calculated cumulative noise exposure. Two issues with the quality of the JEM are explored in more detail below:

4.2.2.3.1 Time Axis in the JEM

The noise measurements in the dataset were collected between 1970 and 2004. About 98% of samples were collected before 1994. However, the period covered by NPHS was from 1994 to 2004. Therefore, if there existed an obvious temporal trend in the noise levels, the mean noise levels before and after 1994 could be different and it would be necessary to add a time (year) axis to the JEM. Restriction of measurements to those after 1994 was not possible as most of the samples were collected before that.

Considering the whole dataset, the noise levels decreased at a rate of 0.15 dBA per year. So the total decrease in the noise level during the 34 years covered by the dataset was 5.1 dBA. The association between noise exposure level and sampling year was negligible ($R^2 = 0.0055$). The temporal trend was also investigated in the following four occupation groups (1-digit NOC-S level, accounts for 98% of all measurements) in which there were enough observations across time to allow for the trend analysis: (1) occupations unique to processing, manufacturing and utilities, (2) trades, transport and equipment and operators and related occupations, (3) occupations unique to primary industry, and (4) sales and service occupations. No obvious increasing or decreasing trend was found in the four occupation groups. So in these groups, the influence from time (year) was weak, indicating that adding the time axis in JEM was not necessary. In other occupation groups where there were small number of observations and cluster of observations in certain time period, the temporal trend based on linear regression could not be assessed. In terms of temporal trend by different industries, a decreasing temporal trend was found in public administration only.

Given the findings above, it was decided that it was not necessary to add a time axis in the JEM for these occupation groups. However, since there was an obvious decreasing temporal trend in public administration industry, biased noise exposure might be estimated in individuals who belonged to this industry category and overestimated exposure could be expected. But in each cycle, only a small proportion of subjects (less than 2%) were assigned a noise level based on their industry code of public administration. The impact on the overall population could be very slight.

4.2.2.3.2 Noise Exposure Levels

The minimum and maximum noise exposure levels collected in the dataset were 50 dBA and 150 dBA, which means this dataset covered occupations/industries with low exposure as well as some exposed to extremely high levels of noise. Considering the mean noise level of 91.4 dBA and distribution of the collected noise levels, the majority of occupations/industries contained in this dataset had relatively high exposure to noise. This is to some extent consistent with the compliance-orientation of the WorkSafeBC's noise exposure dataset. Those occupations and/or industries with more chance of being exposed to high level of noise were more likely to be sampled.

High mean noise exposure levels were found in those occupations or groups of occupations expected to have higher exposure, for example, occupations unique to processing, manufacturing and utilities (92.6 dBA), and occupations unique to primary industry (91.2 dBA). However, for management occupations, the mean noise exposure level (74.6 dBA) seems a little high; typical office exposure would be expected to be around 60 dBA or less. Overestimation of noise levels would result in underestimated ORs, while underestimated noise levels would lead to overestimated ORs.

In terms of noise levels by industries, there was relatively small variance among the calculated mean noise levels by industries (2-digit NAICS level). However, an unexpectedly high mean noise exposure level was found in the education services industry (92.2 dBA). One explanation for this could be that the samples might be collected in trade schools or departments, where the noise levels could be high. Since the WorkSafeBC's noise dataset was compliance oriented, those industries with high levels of noise exposure were more likely to be sampled. And within an industry, occupations having more chance of being exposed to high levels of noise were more likely to be sampled. This indicates that the mean noise levels by occupations may provide a more reasonable and reliable estimation for an individual's noise exposure than by industries. Using the mean noise level of the combination of both occupation and industry should yield the best estimation. Therefore, when linking the noise level to individuals in NPHS, priority was given to noise levels that could be assigned by a combination of both occupation and industry of employment, followed by occupations only, and followed by industries alone.

4.2.2.4 Linking Health and Exposure Stage

The noise levels in the JEM were assigned to each subject in NPHS based on NOC-S and NAICS codes. The confidence of the assignment was ranked one to six based on the level of NAICS or NOC-S codes available; ranks 1 to 4, indicated that the linkage was based on 4-digit NOC-S and/or NAICS, and were considered to provide better noise estimation compared to ranks 5 and 6 (linkage based on 2-digit NOC-S or NAICS). If a subject's noise level in each of eight cycles was assigned at least a rank of 4, the sum of the ranks from all cycles was 32, and we used this as a threshold for a sensitivity test. The main analyses were re-run within subjects whose sum of ranks was 32 or less. For the CVD, the direction of calculated ORs for medium and high exposure groups remained the same while the association did become weaker. For diabetes and RA, the direction of ORs did not change but the association became stronger (though still not statistically significant). This result indicates that the different assigned ranks had some influence on the calculated ORs but the effects were negligible to the overall conclusion.

4.2.2.5 Estimating Cumulative Noise Exposure Stage

The cumulative noise exposure for each subject was estimated based on exposure level (from the JEM) and exposure duration (from the NPHS). Two issues that influenced the validity of the results were selection of exposure metric and missing values.

4.2.2.5.1 Selection of Exposure Metric

In previous studies on the noise – CVD association (Suadicani *et al*., 2012; Gan *et al*., 2011; Gopinath *et al*., 2011; Selander *et al*., 2009; Sbihi *et al*., 2008; McNamee *et al*., 2006; Babisch *et al*., 2005; Davies *et al*., 2005), different exposure metrics were used to estimate people's noise exposure. In general, there were two major methods, subjective and objective. In the former method, the subjects report whether they think they were exposed to noise and how many years they were exposed. Therefore, the reported information could be regarded as qualitative and less accurate. The objective method measured the exposed noise level of subjects and is able to provide a more accurate estimation. Despite the likely more accurate estimation of noise exposure intensity using objective methods, some argue that if the noise-disease association is mainly based on the stress response and the response is susceptible to personal parameters (e.g. personal susceptibility to noise, attitude to the noise), the subjective method is able to adjust for these parameters and better reflects the stress response (Babisch, 1998). Neitzel *et al*. (2009) compared the perceived and quantitative measures of occupational noise exposure and found that using the subjective assessment might improve the contrast and precision of epidemiological exposure estimates for workers with highly variable noise exposure. They also suggested combining the subjective and objective estimates to reduce bias and improve precision.

In this study, the cumulative noise exposure combined measured exposure levels from a JEM and exposure duration estimated from self-reported job history. Because there was no question in the NPHS regarding the subjects' subjective perception of workplace noise, subjective noise exposure was not assessed in our study.

The cut points for different exposure groups were selected mainly to ensure enough cases in each exposure group (or the results can not be released). However, in previous studies, increased secretion of stress hormones (e.g. adrenaline, nordrenaline, cortisol) was found in subjects exposed to occupational noise and threshold for the increased secretion was around 60 to 80 dBA (Ising and Braun, 2000; Melamed *et al*., 1996; Sudo *et al*., 1996; Cavatorta *et al*., 1987). This indicated that the cut points in the current study might not be able to distinguish the unexposed group and low exposure group. An analysis was done re-categorizing subjects into a definite unexposed group (<60 dBA, around 20% of all subjects) and a possible or definite exposed group (e.g. "ever/never"). This method was also suggested by Dosemeci and Stewart (1996) to reduce exposure misclassification by placing the subjects whose exposure status was in doubt into the category with the largest number of subjects. For CVD, the results of the multiple regression using this metric showed an OR of 1.2 (95% CI: 0.8 – 1.9) for the possible or definite exposed group though it was not statistically significant. For diabetes, the ORs for the exposed group were 0.9 (95% CI: 0.7 – 2.74) (The noise and RA association became stronger. However, the results can not be released due to limited sample size as the definite unexposed group was only a fraction of the original low exposure group). This crude estimation based on NOC-S codes may have reduced misclassification and revealed a result that was more consistent with previous studies of CVD.

4.2.2.5.2 Missing Values

In order to examine the influence from missing values in the exposure assessment, sensitivity tests were conducted. The proportion of subjects who did not have any missing values in the four variables (MEAN, HOUR, WEEK, TWOYEAR, detail shown in Section 2.8.2) needed for estimating the CNE across the eight cycles over the total subjects for diabetes, RA, and CVD were all around 50%. When estimated through person-year, the proportion of missing exposure period over total exposure period for diabetes, RA, and CVD were 28%, 21%, and 28% respectively. When re-running the multi-variable conditional logistic regression restricted to subjects who did not have any missing values in the four variables across the eight cycles, the direction of the ORs for different exposure groups remained the same, but there was a relatively

large change in the magnitude of the ORs (Results can not be released due to small sample size). Given the relatively large number of subjects with missing values affecting exposure assessment and the stronger association with improved exposure assessment, it might be inferred that the missing values may have resulted in a misclassification bias that attenuated observed results.

4.2.3 Hearing Protectors

The issues related to hearing protection devices (HPD) are discussed in the introduction section. In the current study, lack of information on hearing protectors among subject in the NPHS meant that we could not adjust for their influence. Wearing hearing protectors is more likely to influence subjects who had relatively high noise exposures at work. Therefore, without information on hearing protectors, some subjects who worked in noisy environments, and wore HPD and whose real exposure was therefore moderate (and who should have been in the medium exposure group) may have been categorized into the high exposure group. An analysis was conducted merging the medium and high exposure groups into one. For the three health outcomes of interest, the calculated ORs for this new exposure group were very close to one and not statistically significant, indicating the impact of wearing hearing protectors could be mild.

4.2.4 Healthy Worker Effect

The healthy worker effect is another source of bias. Workers with certain disease outcomes may die of the disease or leave their positions due to the impact of the disease on their ability to work. Moreover, people who are susceptible to noise and those who already had some disease symptoms may not be willing to work in a noisy environment (Babisch, 1998). This is more likely to be the case for the outcome of CVD and RA compared to diabetes because CVD may result in more severe outcomes which restrain workers' daily activities. The healthy worker effect would dilute the magnitude of the effect estimate and bias the estimates towards the null.

4.3 Strengths and Limitations

4.3.1 Strengths

There were very few previous studies focusing on the association between noise exposure and the health outcomes of diabetes and RA. Though the biological plausibility was studied and proposed based on some experimental studies, information on the past population-based studies was missing to support the biological mechanism. This study is the first to investigate the direct association between occupational noise and diabetes and RA. Although no significant association was found, it laid the basis and provided some implications for future studies.

Most previous studies focusing on occupational noise selected workers in a certain industry as the study population to form a relatively homogeneous occupational group. This is to some extent supported by Babisch's (1998) argument on white and blue collar workers. He argued that the working environment could be quite different between white collar workers and blue collar workers. Many factors (e.g. heat, cold, organic solvents) in the workplace were associated with noise exposure and also possibly related to the health outcome. Moreover, white and blue collar workers differ in lifestyle, socio-economic status, etc. All these factors may play a role as potential confounders and therefore, a relatively homogeneous occupational group was preferred to reduce the impact of confounding on the relationship between noise and disease. However, a narrow study population may compromise the generalizability of the study results. Previous studies using the general population to estimate the noise-CVD association found positive results (Gan *et al*., 2011; Gopinath *et al*., 2011). Although the generalizablity of the current study was restricted because survey weights were not applied to the findings, various occupations were included in the NPHS covering both white collar workers and blue collar workers. Furthermore, with sufficient information provided on subjects' lifestyle and socio-economic status, the effects of the potential confounders were adjusted in the regression model.

WorkSafeBC's noise exposure dataset provided noise levels in a wide variety of occupations and industries, which enabled quantitative exposure assessment for subjects in the NPHS. Given the large number of observations in the noise exposure dataset, it provided a relatively reliable estimation of the noise level in certain occupations and industries. Although the distribution of noise samples was skewed towards certain occupations and industries (e.g. manufacturing industries and occupations unique to them), even in those occupations/industries where the number of samples was small (n around 10), the number of samples was still larger than some studies using only very few or even single noise measurement to quantify exposure (Chang *et al*., 2009a; Chang *et al*., 2009b; Lee *et a*l., 2009; Selander *et al*., 2009).

4.3.2 Limitations

Many of the most important limitations have been discussed in the prior section on bias.

Although the NPHS subjects were a representative sample of Canadian population in 1994/1995, the study samples used were subsamples of the original population. Inclusion/exclusion criteria were applied for the purposes of these analyses and cases and controls were selected from the study cohort. Moreover, a large number of NPHS subjects were dropped due to unknown disease status (diabetes: N = 2,308, RA: N = 2,224, CVD: N = 2,303). Comparison between them and the study subjects of the current study (both cases and controls) showed that they were younger and they were more likely to have lower education and income. Therefore, selection bias was possible and may have some impact on the external validity.

Some previous studies found that many other work-related factors may have joint effects with noise on the risk of health outcomes. Co-exposure of noise with air pollutants (e.g. particulate matter, nitrogen dioxide, nitric oxide), organic solvents, and job strain may increase the risk of CVD and we did not have data on these co-exposures (Gan *et al*., 2012; Beelen *et al*., 2009; Selander *et al*., 2009; Chang *et al*., 2009a; Chang *et al*., 2009b; Selander *et al*., 2007). For the health outcome of diabetes and RA, although no previous studies have been conducted to suggest the existence of joint effects, given their similar pathophysiological mechanism and the general

noise-disease biological model, it is quite possible that the joint effect of other factors with noise on diabetes and/or RA may exist. However, due to lack of information on relevant factors, joint effects were not considered in this study.

Another limitation in the current study relates to Statistics Canada's policy to protect participants' privacy by limiting the reporting of findings based on small cell sizes. Results based on fewer than 15 respondents do not meet the requirement and are not eligible for disclosure. Therefore, some categories were collapsed for the analysis, including for example, the three different classes of obesity were merged into the "obese" category for CVD and RA due to small sample sizes, and the "occasional drinker" and "never drank" categories were collapsed into one for diabetes and CVD. Due to the collapse of categories, the dose-response relationship between health outcome and covariates might be diluted or distorted and this may also influence the effects in the multiple regression model. However, the influence is expected to be mild.

4.4 Future Perspectives

No statistically significant associations were found between occupational noise exposure and the health outcomes of diabetes, RA, and CVD as we hypothesized. Because the quality of the noise exposure assessment in this study is uncertain, and sensitivity tests suggested that improvements to the exposure assessment influenced the strength of association, further studies are needed to assess these associations, especially for diabetes and RA, given the sparse evidence from previous studies. There are some issues that future researchers should consider.

(1) Selection of exposure metric: Given the stress response as the biological basis for the noise-disease association, using a subjective metric does have some advantages in incorporating the personal parameters that can influence the stress response. But its estimates are crude compared to the objective metric, which is able to provide a relatively accurate quantitative assessment of noise exposure. There is no conclusion about which one is better and it deserves further study to investigate how to integrate the two methods.

(2) Other sources of noise exposure: Noise exists almost everywhere in people's daily life. The exposure from workplace only contributes a proportion of the total exposure. Although noise from other sources (e.g. traffic noise, MP3 players) may not be as stable or as high as occupational noise, its contribution should not be ignored especially if it is more frequent.

(3) Joint effects or "side pathways": There are other factors that may have joint effects with noise on the disease outcome. It is a point worth exploring and its results may contribute to understanding mechanisms of the proposed biological model. Also side pathways may exist beside the stress response model. For example, the noise exposure in the workplace may modify workers' lifestyles and further influence the health outcome.

(4) Using the general population as study population: Although this study did not find positive associations between occupational noise exposure and the three health outcomes of interest, our attitude about using the general population to study the noise-disease association in future studies is positive, given the strengths of using the general population (better generalizability, sufficient information on potential confounders) and previous positive studies based on general population samples.

Although no positive results were found in this study, considering the biological plausibility of the associations between noise exposure and a variety of well-demonstrated and potential health outcomes (e.g. noise-induced hearing loss, sleep disturbance, CVD, diabetes, RA) and the ubiquitous nature of noise exposure, the relationship between noise and disease outcomes warrants further attention by policy makers, researchers, and other relevant health professionals. Studies should be conducted to assess the effectiveness of hearing conservation programs to see if any improvement can be made to allow them to cost-effectively reach their aims. Relevant policies or bylaws should be reinforced to lower the noise exposure not only in occupational but also in environmental scenarios (traffic noise, community noise, etc). There are also responsibilities of engineers to improve current engineering control methods or design more effective methods to control noise, preferably at the source.

4.5 Conclusions

No statistically significant associations were found between occupational noise exposure and the two major health outcomes of interest, diabetes and RA. However, in the main sensitivity analysis, the study on the noise - CVD association, no positive associations were found. There are multiple possible explanations for the negative findings: 1) the negative results could result from study biases such as misclassification in exposure and/or the health outcome; or 2) there was no real association between noise and the health outcomes. It seems more likely that biases diluted the measured association, given the large amount of evidence from previous studies, especially for CVD. As for diabetes and rheumatoid arthritis, given the possible biases in this study and limited evidence from previous studies, future studies are warranted to improve the exposure assessment methods to investigate the hypothesized relationship between noise and the two disease outcomes.

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Appendices

Appendix A:

Temporal Trend of Noise Levels by Different Occupations / Industries

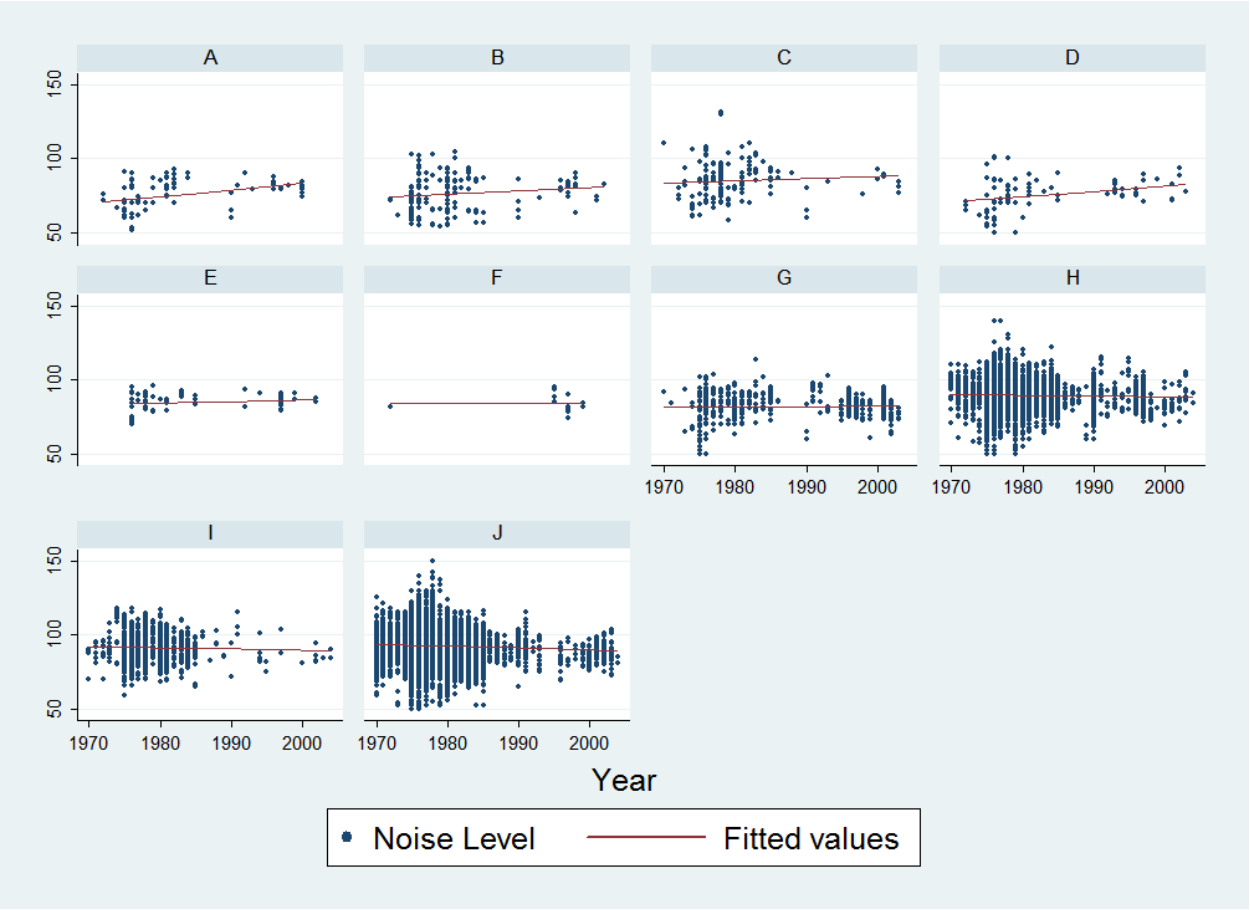

Figure A. 1 Temporal Trend of Noise Level by Occupations

A – Management Occupations;
B – Business, Finance and Administrative Occupations;
C – Natural and Applied Sciences and Related Occupations;
D – Health Occupations;
E – Occupations in Social Science, Education, Government Service and Religion;
F –Occupations in Art, Culture, Recreation and Sport;
G – Sales and Service Occupations;
H – Trades, Transport and Equipment Operators and Related Occupations;
I – Occupations Unique to Primary Industry;
J – Occupations Unique to Processing, Manufacturing and Utilities.

Figure A. 2 Temporal Trend of Noise Levels by Industries

11 – Agriculture, Forestry, Fishing and Hunting;
21 – Mining, Quarrying, and Oil and Gas Extraction;
22 – Utilities;
23 – Construction;
31 / 32 / 33 – Manufacturing;
41 – Wholesale Trade;
44 / 45 – Retail Trade;
48 / 49 – Transportation and Warehousing;
51 – Information and Cultural Industries;
52 – Finance and Insurance;
53 – Real Estate and Rental and Leasing;
54 – Professional, Scientific and Technical Services;
56 – Administrative and Support, Waste Management and Remediation Services;
61 – Educational Services;
62 – Health Care and Social Assistance;
71 – Arts, Entertainment and Recreation;
72 – Accommodation and Food Services;
81 – Other Services (except Public Administration);
91 – Public Administration.

Appendix B:

The Model Selection Process

Table B. 1 Model Selection Process for Diabetes

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
		Model 1	Model 2
Exposure			
Low-exposure (< 85 dBA-year)	1	1	1
Medium-exposure (85 – 95 dBA-year)	0.92 (0.62 – 1.36)	0.90 (0.61 - 1.34)	0.91 (0.60 - 1.38)
High-exposure (>95 dBA-year)	0.94 (0.63 – 1.40)	0.94 (0.63 - 1.41)	1.02 (0.67 - 1.56)
Obese Status			
Underweight / Normal Weight	1		1
Overweight	2.06 (1.27 – 3.34)		2.14 (1.31 - 3.49)
Obese I	4.22 (2.53 – 7.01)		4.24 (2.53 - 7.09)
Obese II	7.72 (4.02 – 14.83)		7.60 (3.91 - 14.75)
Obese III	9.46 (4.39 – 20.36)		8.67 (3.94 - 19.07)
Physical Activity			
Active	1		
Moderate	1.01 (0.65 – 1.58)		
Inactive	1.73 (1.17 – 2.54)		
Smoke			
Never Smoked	1		
Former Smoker	1.16 (0.81 – 1.66)		
Current Smoker	0.97 (0.62 – 1.52)		
Drinking Status			
Occasional Drinker / Never Drank	1		
Former Drinker	1.01 (0.62 - 1.65)		
Regular Drinker	0.55 (0.38 - 0.81)		
Hypertension at Cycle 1			
No	1		
Yes	2.67 (1.64 – 4.34)		
Education			
Less than Secondary School	1	1	1
Graduation			
Secondary School Graduation	1.32 (0.78 – 2.26)	1.42 (0.82 - 2.43)	1.50 (0.85 - 2.63)
Some Post-secondary	1.09 (0.68 – 1.72)	1.19 (0.74 - 1.92)	1.33 (0.81 - 2.16)
Post-secondary Graduation	0.71 (0.45 – 1.12)	0.85 (0.53 - 1.36)	0.95 (0.59 - 1.53)
Family Income			
< $40,000	1	1	1
$ 40,000 - $ 79,999	1.02 (0.70 – 1.48)	1.00 (0.68 - 1.46)	1.05 (0.70 - 1.56)
> $ 80,000	0.57 (0.37 – 0.87)	0.61 (0.39 - 0.94)	0.68 (0.43 - 1.08)

Table B. 1 Model Selection Process for Diabetes (continued)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
		Model 3	Model 4
Exposure			
Low-exposure (< 85 dBA-year)	1	1	1
Medium-exposure (85 – 95 dBA-year)	0.92 (0.62 – 1.36)	0.90 (0.59 - 1.37)	0.90 (0.59 - 1.37)
High-exposure (>95 dBA-year)	0.94 (0.63 – 1.40)	1.02 (0.67 - 1.56)	1.02 (0.67 - 1.56)
Obese Status			
Underweight / Normal Weight	1	1	1
Overweight	2.06 (1.27 – 3.34)	2.16 (1.32 - 3.52)	2.18 (1.33 - 3.56)
Obese I	4.22 (2.53 – 7.01)	4.21 (2.52 - 7.05)	4.29 (2.55 - 7.23)
Obese II	7.72 (4.02 – 14.83)	7.53 (3.85 - 14.73)	7.67 (3.90 - 15.08)
Obese III	9.46 (4.39 – 20.36)	8.21 (3.69 - 18.25)	8.33 (3.70 - 18.72)
Physical Activity			
Active	1	1	1
Moderate	1.01 (0.65 – 1.58)	0.92 (0.58 - 1.47)	0.92 (0.58 - 1.48)
Inactive	1.73 (1.17 – 2.54)	1.44 (0.96 - 2.17)	1.43 (0.95 - 2.16)
Smoke			
Never Smoked	1		1
Former Smoker	1.16 (0.81 – 1.66)		1.07 (0.73 - 1.57)
Current Smoker	0.97 (0.62 – 1.52)		1.15 (0.71 - 1.87)
Drinking Status			
Occasional Drinker / Never Drank	1		
Former Drinker	1.01 (0.62 - 1.65)		
Regular Drinker	0.55 (0.38 - 0.81)		
Hypertension at Cycle 1			
No	1		
Yes	2.67 (1.64 – 4.34)		
Education			
Less than Secondary School	1	1	1
Graduation			
Secondary School Graduation	1.32 (0.78 – 2.26)	1.50 (0.85 - 2.64)	1.52 (0.86 - 2.68)
Some Post-secondary	1.09 (0.68 – 1.72)	1.33 (0.82 - 2.17)	1.34 (0.82 - 2.19)
Post-secondary Graduation	0.71 (0.45 – 1.12)	0.98 (0.60 - 1.58)	0.99 (0.61 - 1.61)
Family Income			
< $40,000	1	1	1
$ 40,000 - $ 79,999	1.02 (0.70 – 1.48)	1.13 (0.75 - 1.69)	1.13 (0.76 - 1.71)
> $ 80,000	0.57 (0.37 – 0.87)	0.75 (0.47 - 1.19)	0.75 (0.47 - 1.20)

Table B. 1 Model Selection Process for Diabetes (continued)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
		Model 5	Model 6
Exposure			
Low-exposure (< 85 dBA-year)	1	1	1
Medium-exposure (85 – 95 dBA-year)	0.92 (0.62 – 1.36)	0.91 (0.60 - 1.39)	0.93 (0.61 - 1.41)
High-exposure (>95 dBA-year)	0.94 (0.63 – 1.40)	1.03 (0.67 - 1.58)	1.04 (0.67 - 1.59)
Obese Status			
Underweight / Normal Weight	1	1	1
Overweight	2.06 (1.27 – 3.34)	2.16 (1.32 - 3.54)	2.14 (1.31 - 3.51)
Obese I	4.22 (2.53 – 7.01)	4.17 (2.48 - 7.02)	4.03 (2.39 - 6.80)
Obese II	7.72 (4.02 – 14.83)	7.31 (3.71 - 14.43)	6.88 (3.47 - 13.67)
Obese III	9.46 (4.39 – 20.36)	7.68 (3.40 - 17.31)	7.4 (3.26 - 16.80)
Physical Activity			
Active	1	1	1
Moderate	1.01 (0.65 – 1.58)	0.92 (0.58 - 1.48)	0.93 (0.58 - 1.49)
Inactive	1.73 (1.17 – 2.54)	1.41 (0.94 - 2.12)	1.37 (0.91 - 2.06)
Smoke			
Never Smoked	1	1	1
Former Smoker	1.16 (0.81 – 1.66)	1.10 (0.75 - 1.61)	1.09 (0.74 - 1.59)
Current Smoker	0.97 (0.62 – 1.52)	1.19 (0.73 - 1.94)	1.22 (0.75 - 1.99)
Drinking Status			
Occasional Drinker / Never Drank	1	1	1
Former Drinker	1.01 (0.62 - 1.65)	0.99 (0.59 - 1.66)	1.01 (0.60 - 1.71)
Regular Drinker	0.55 (0.38 - 0.81)	0.71 (0.46 - 1.08)	0.74 (0.48 - 1.14)
Hypertension at Cycle 1			
No	1		1
Yes	2.67 (1.64 – 4.34)		1.62 (0.94 - 2.78)
Education			
Less than Secondary School	1	1	1
Graduation			
Secondary School Graduation	1.32 (0.78 – 2.26)	1.56 (0.88 - 2.77)	1.60 (0.90 - 2.84)
Some Post-secondary	1.09 (0.68 – 1.72)	1.38 (0.84 - 2.25)	1.37 (0.84 - 2.25)
Post-secondary Graduation	0.71 (0.45 – 1.12)	1.03 (0.63 - 1.68)	1.05 (0.64 - 1.72)
Family Income			
< $40,000	1	1	1
$ 40,000 - $ 79,999	1.02 (0.70 – 1.48)	1.22 (0.81 - 1.85)	1.21 (0.80 - 1.84)
> $ 80,000	0.57 (0.37 – 0.87)	0.84 (0.52 - 1.37)	0.86 (0.53 - 1.39)

Table B. 2 Model Selection Process for Rheumatoid Arthritis

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
		Model 1	Model 2
Exposure			
Low-exposure (< 85 dBA-year)	1	1	1
Medium-exposure (85 – 95 dBA-year)	0.95 (0.54 – 1.68)	1.01 (0.57 - 1.82)	1.01 (0.56 - 1.81)
High-exposure (>95 dBA-year)	0.93 (0.51 – 1.70)	1.05 (0.56 - 1.96)	1.03 (0.55 - 1.94)
Obese Status			
Underweight / Normal Weight	1		
Overweight	1.09 (0.63 – 1.86)		
Obese	1.08 (0.60 - 1.96)		
Physical Activity			
Active	1		
Moderate	0.57 (0.30 - 1.08)		
Inactive	0.91 (0.54 - 1.52)		
Smoke			
Never Smoked	1		1
Former Smoker	1.67 (0.87 - 3.21)		1.04 (0.59 - 1.82)
Current Smoker	1.17 (0.67 - 2.01)		1.44 (0.73 - 2.83)
Education			
Secondary School Graduation or Less	1	1	1
Some Post-secondary	1.53 (0.84 - 2.77)	1.71 (0.93 - 3.13)	1.76 (0.96 - 3.24)
Post-secondary Graduation	0.74 (0.41 - 1.31)	0.85 (0.47 - 1.55)	0.90 (0.49 - 1.64)
Family Income			
< $40,000	1	1	1
$ 40,000 - $ 79,999	0.90 (0.49 - 1.62)	0.97 (0.53 - 1.78)	0.99 (0.54 - 1.82)
> $ 80,000	0.48 (0.26 - 0.90)	0.51 (0.27 - 0.97)	0.53 (0.28 - 1.00)

Table B. 2 Model Selection Process for Rheumatoid Arthritis (continued)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
		Model 3	Model 4
Exposure			
Low-exposure (< 85 dBA-year)	1	1	1
Medium-exposure (85 – 95 dBA-year)	0.95 (0.54 – 1.68)	1.01 (0.56 - 1.82)	1.01 (0.56 - 1.82)
High-exposure (>95 dBA-year)	0.93 (0.51 – 1.70)	1.04 (0.55 - 1.94)	1.07 (0.57 - 2.01)
Obese Status			
Underweight / Normal Weight	1	1	1
Overweight	1.09 (0.63 – 1.86)	1.11 (0.64 - 1.92)	1.09 (0.63 - 1.90)
Obese	1.08 (0.60 - 1.96)	1.09 (0.59 - 2.00)	1.11 (0.59 - 2.08)
Physical Activity			
Active	1		1
Moderate	0.57 (0.30 - 1.08)		0.48 (0.25 - 0.93)
Inactive	0.91 (0.54 - 1.52)		0.76 (0.44 - 1.32)
Smoke			
Never Smoked	1	1	1
Former Smoker	1.67 (0.87 - 3.21)	1.03 (0.59 - 1.81)	1.00 (0.56 - 1.78)
Current Smoker	1.17 (0.67 - 2.01)	1.43 (0.73 - 2.83)	1.48 (0.75 - 2.94)
Education			
Secondary School Graduation or Less	1	1	1
Some Post-secondary	1.53 (0.84 - 2.77)	1.77 (0.96 - 3.25)	1.86 (1.01 - 3.44)
Post-secondary Graduation	0.74 (0.41 - 1.31)	0.89 (0.49 - 1.63)	0.91 (0.50 - 1.66)
Family Income			
< $40,000	1	1	1
$ 40,000 - $ 79,999	0.90 (0.49 - 1.62)	0.99 (0.54 - 1.82)	0.98 (0.53 - 1.80)
> $ 80,000	0.48 (0.26 - 0.90)	0.53 (0.28 - 1.01)	0.50 (0.26 - 0.96)

Table B. 3 Model Selection Process for Cardiovascular Disease

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
		Model 1	Model 2
Exposure			
Low-exposure (< 85 dBA-year)	1	1	1
Medium-exposure (85 – 95 dBA-year)	0.87 (0.61 – 1.26)	0.87 (0.60 - 1.27)	0.86 (0.59 - 1.24)
High-exposure (>95 dBA-year)	0.77 (0.53 – 1.14)	0.80 (0.54 - 1.18)	0.80 (0.54 - 1.18)
Obesity Status			
Underweight / Normal Weight	1		1
Overweight	1.08 (0.75 - 1.55)		1.10 (0.76 - 1.59)
Obese	1.39 (0.95 - 2.04)		1.35 (0.92 - 2.01)
Physical Activity			
Active	1		
Moderate	0.71 (0.47 – 1.08)		
Inactive	1.05 (0.73 – 1.50)		
Smoke			
Never Smoked	1		
Former Smoker	1.76 (1.21 – 2.56)		
Current Smoker	1.40 (0.87 – 2.24)		
Drinking Status			
Occasional / Never Drank	1		
Former Drinker	1.08 (0.69 - 1.70)		
Regular Drinker	0.64 (0.45 - 0.92)		
Hypertension at Cycle 1			
No	1		
Yes	2.73 (1.71 – 4.36)		
Education			
Less than Secondary School Graduation	1	1	1
Secondary School Graduation	0.80 (0.47 – 1.34)	0.85 (0.50 - 1.44)	0.88 (0.52 - 1.49)
Some Post-secondary	0.89 (0.57 – 1.40)	1.00 (0.63 - 1.58)	1.03 (0.65 - 1.63)
Post-secondary Graduation	0.67 (0.44 – 1.02)	0.84 (0.54 - 1.31)	0.86 (0.55 - 1.34)
Family Income			
< $40,000	1	1	1
$ 40,000 - $ 79,999	0.87 (0.61 – 1.24)	0.89 (0.62 - 1.28)	0.89 (0.62 - 1.28)
> $ 80,000	0.46 (0.31 – 0.68)	0.48 (0.32 - 0.74)	0.49 (0.32 - 0.75)

Table B. 3 Model Selection Process for Cardiovascular Disease (continued)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
		Model 3	Model 4
Exposure			
Low-exposure (< 85 dBA-year)	1	1	1
Medium-exposure (85 – 95 dBA-year)	0.87 (0.61 – 1.26)	0.86 (0.59 - 1.24)	0.85 (0.59 - 1.24)
High-exposure (>95 dBA-year)	0.77 (0.53 – 1.14)	0.80 (0.54 - 1.18)	0.80 (0.54 - 1.19)
Obesity Status			
Underweight / Normal Weight	1	1	1
Overweight	1.08 (0.75 - 1.55)	1.13 (0.78 - 1.63)	1.09 (0.75 - 1.58)
Obese	1.39 (0.95 - 2.04)	1.34 (0.90 - 1.99)	1.29 (0.86 - 1.92)
Physical Activity			
Active	1	1	1
Moderate	0.71 (0.47 – 1.08)	0.69 (0.45 - 1.06)	0.69 (0.45 - 1.05)
Inactive	1.05 (0.73 – 1.50)	0.93 (0.64 - 1.36)	0.95 (0.65 - 1.39)
Smoke			
Never Smoked	1		1
Former Smoker	1.76 (1.21 – 2.56)		1.73 (1.19 - 2.54)
Current Smoker	1.40 (0.87 – 2.24)		1.23 (0.76 - 2.00)
Drinking Status			
Occasional / Never Drank	1		
Former Drinker	1.08 (0.69 - 1.70)		
Regular Drinker	0.64 (0.45 - 0.92)		
Hypertension at Cycle 1			
No	1		
Yes	2.73 (1.71 – 4.36)		
Education			
Less than Secondary School	1	1	1
Graduation			
Secondary School Graduation	0.80 (0.47 – 1.34)	0.89 (0.53 - 1.51)	0.95 (0.56 - 1.61)
Some Post-secondary	0.89 (0.57 – 1.40)	1.05 (0.66 - 1.67)	1.07 (0.67 (1.70)
Post-secondary Graduation	0.67 (0.44 – 1.02)	0.88 (0.56 - 1.38)	0.92 (0.59 - 1.46)
Family Income			
< $40,000	1	1	1
$ 40,000 - $ 79,999	0.87 (0.61 – 1.24)	0.89 (0.62 - 1.28)	0.87 (0.60 - 1.26)
> $ 80,000	0.46 (0.31 – 0.68)	0.49 (0.32 - 0.75)	0.47 (0.31 - 0.72)

Table B. 3 Model Selection Process for Cardiovascular Disease (continued)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
		Model 5	Model 6
Exposure			
Low-exposure (< 85 dBA-year)	1	1	1
Medium-exposure (85 – 95 dBA-year)	0.87 (0.61 – 1.26)	0.89 (0.61 - 1.30)	0.87 (0.59 - 1.28)
High-exposure (>95 dBA-year)	0.77 (0.53 – 1.14)	0.83 (0.56 - 1.24)	0.85 (0.57 - 1.27)
Obesity Status			
Underweight / Normal Weight	1	1	1
Overweight	1.08 (0.75 - 1.55)	1.12 (0.77 - 1.63)	1.12 (0.77 - 1.63)
Obese	1.39 (0.95 - 2.04)	1.28 (0.86 - 1.90)	1.18 (0.79 - 1.78)
Physical Activity			
Active	1	1	1
Moderate	0.71 (0.47 – 1.08)	0.67 (0.44 - 1.03)	0.65 (0.42 - 1.01)
Inactive	1.05 (0.73 – 1.50)	0.91 (0.62 - 1.34)	0.91 (0.62 - 1.34)
Smoke			
Never Smoked	1	1	1
Former Smoker	1.76 (1.21 – 2.56)	1.81 (1.23 - 2.66)	1.81 (1.23 - 2.67)
Current Smoker	1.40 (0.87 – 2.24)	1.29 (0.79 - 2.11)	1.30 (0.80 - 2.13)
Drinking Status			
Occasional / Never Drank	1	1	1
Former Drinker	1.08 (0.69 - 1.70)	1.04 (0.66 - 1.66)	1.03 (0.64 - 1.65)
Regular Drinker	0.64 (0.45 - 0.92)	0.68 (0.47 - 1.00)	0.68 (0.46 - 1.00)
Hypertension at Cycle 1			
No	1		1
Yes	2.73 (1.71 – 4.36)		2.86 (1.74 - 4.69)
Education			
Less than Secondary School Graduation	1	1	1
Secondary School Graduation	0.80 (0.47 – 1.34)	0.99 (0.58 - 1.69)	1.00 (0.59 - 1.71)
Some Post-secondary	0.89 (0.57 – 1.40)	1.11 (0.70 - 1.78)	1.12 (0.70 - 1.80)
Post-secondary Graduation	0.67 (0.44 – 1.02)	0.97 (0.61 - 1.54)	0.96 (0.60 - 1.52)
Family Income			
< $40,000	1	1	1
$ 40,000 - $ 79,999	0.87 (0.61 – 1.24)	0.91 (0.63 - 1.33)	0.95 (0.65 - 1.39)
> $ 80,000	0.46 (0.31 – 0.68)	0.52 (0.33 - 0.80)	0.52 (0.34 - 0.81)