ASSESSING THE IMPACTS OF TRAFFIC-RELATED AND WOODSMOKE PARTICULATE MATTER ON SUBCLINICAL MEASURES OF CARDIOVASCULAR HEALTH: A HEPA FILTER INTERVENTION STUDY

by

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Abstract

Fine particulate matter (PM$_{2.5}$) plays an important role in the link between air pollution and a range of health effects including respiratory and cardiovascular morbidity and mortality. The specific sources of PM$_{2.5}$ responsible for these effects have not been definitively identified. With traffic-related air pollution (TRAP) and woodsmoke (WS) as two of the major contributors to ambient PM$_{2.5}$ concentrations, this study was the first to investigate the difference in health outcomes between these two sources. The purpose of this study was to compare cardiovascular exposure-response relationships for TRAP and WS and to evaluate the impact of HEPA filtration on indoor TRAP and WS PM$_{2.5}$ levels.

In this single-blind randomized crossover study, 83 healthy adults (54 living in high TRAP and 29 living in high WS areas) between the ages of 19 and 72 living in Metro Vancouver were recruited. Areas with high TRAP or high WS were identified using previously developed spatial models and subjects were recruited by letters sent to households in these areas. Sampling was conducted over two consecutive one-week periods, one with filtration and one with no filtration. Two filtration devices were used, one in the main living room and one in main bedroom. Endothelial function was measured at the end of each week and blood was drawn at baseline and at the end of each week. Mixed effect models were used to investigate the relationship between exposure and outcome variables.

Overall, HEPA filtration was associated with a 40% decrease in indoor PM$_{2.5}$ concentrations. There was inconclusive evidence on the potential relationship between TRAP or WS PM$_{2.5}$ exposure and endothelial function. However, there was some suggestion of an association between PM$_{2.5}$ exposure and CRP specifically among male participants in high-TRAP locations (20.6% increase in CRP levels per unit median increase in PM$_{2.5}$, 95% CI, 2.62% – 41.7%). There was no association between any exposure indicators and IL-6 or BCC. In summary, the results support the hypothesis that HEPA filtration can be effective in reducing indoor PM$_{2.5}$
concentrations with some support for the *a priori* hypothesis of a greater impact on markers of inflammation in areas of high TRAP.
Preface

This study was conducted as a collaborative effort between the University of British Columbia and Simon Fraser University. All research described in this dissertation was conducted under the approval of Simon Fraser University Research Ethics Boards (2011a0431). As per the evaluation by UBC Research Ethics Boards, the approval obtained from SFU was recognized by UBC and sufficient for the purposes of this study.
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List of Abbreviations

BCC – Band cell counts
BMI – Body mass index
CHD – Coronary heart disease
CO - Carbon monoxide
CRP – C-reactive protein
CVD – Cardiovascular Disease
DALY – Disability adjusted life years
EC – Elemental carbon
GC-MS – Gas chromatography mass spectroscopy
HEPA – High efficiency particulate air filter
hs-CRP – High sensitivity C-reactive protein
IARC – International Agency for Research on Cancer
IL-6 – Interleukin 6
Kg/m² – Kilograms per square meter
L - Liter
LG – Levoglucosan
LOD – Limit of detection
m² – Meter square
mmHg – Millimeters mercury
PAT – Peripheral arterial tonometry
PM – Particulate Matter
PM₁₀₂ – Particulate matter smaller than 2.5 microns
PMN – Polymorphonuclear leukocytes
%PMN – Percent polymorphonuclear leukocytes
PWA – Pulse wave amplitude
QC – Quality control
RH – Relative humidity
RHI – Reactive hyperemia index
RWC – Residential wood combustion
SD – Standard deviation
SOP – Standard operating procedure
SPPH – School of Population and Public Health
TRAP – Traffic-related air pollution
WS – Woodsmoke
µg – Micro grams
µg/m³ – Micro grams per cubic meter
µm – Micro meter
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Dedication

“The family is one of nature's masterpieces” – George Santayana

To my lovely parents, Mohammad and Shohreh, and awesome siblings, Behrad and Kiana.
1 Introduction

A number of events in the 20th century have revealed the significance of exposure to air pollution among the general public and the scientific community. One of the first well-documented events occurred in December of 1930 over the span of five days in the Meuse Valley of Belgium, at the time the most industrialized region of Europe. As a result of stable atmospheric conditions and industrial emissions, a thick fog covered a great area of the region. Starting from the third day of the fog, scores of people exhibited severe respiratory symptoms. Over 60 people died in a period of three days, which was more than 10 times the normal mortality rate for the region (Nemery, Hoet, & Nemmar, 2001).

In 1948, the first publicized air pollution event in the United States was recorded. Due to residential and industrial emissions in Donora, Pennsylvania and a temperature inversion, about half of the 14,000 population of the town became ill and 20 died, 6 times the normal mortality rate (Helfand, Lazarus, & Theerman, 2001). Finally, in the best known and most severe air pollution episode of the 20th century, over 4,000 excess deaths were reported when London, England was covered with dense smog from December 5th to December 9th in 1952 (Ministry of Health, 1954). Subsequent analyses of the London smog episode have reported over 12,000 excess deaths as a result of acute and longer term exposures to high levels of air pollution (Bell & Davis, 2001).

With the extensive news coverage of each of these air pollution episodes, it became clear to the public that air pollution was responsible for these deaths. Moreover, many individuals realized that even short-term exposures could have detrimental effects on their health. In all three of the events mentioned above, immediate investigations were carried out, which confirmed the association between short-term exposure to high levels of air pollution and increased morbidity and mortality at a population level (Holgate, Koren, Samet, & Maynard, 1999).
It was only after the London smog that significant efforts were initiated to understand the relationship between exposure to various components of air pollution and their potential effect on health. More recently, among other pollutants, most of the focus has been on exposure to particulate matter (PM) as more evidence has unveiled the significant contribution of PM to various serious health effects with acute and chronic exposures (Pope & Dockery, 2006). Given the fact that air pollution exposure is ubiquitous with no safe exposure threshold (Pope & Dockery, 2006), it can be considered as a serious public health issue that could affect anyone regardless of their socioeconomic status, age, sex, etc. Over the past four decades, various measures have been introduced to reduce PM emissions including motor vehicle engine re-design, more stringent emission regulations, and improvements in fuel quality. These measures have significantly reduced air pollution/PM exposure in North America and Western Europe (van Erp, O’Keefe, Cohen, & Warren, 2008). However, high air pollution levels are still widely present in developing countries such as China and India. In China with a rapidly expanding economy, there have been extreme increases in air pollutant emissions across much of the country. With a growing need for energy and reliance on coal for meeting 75% of the energy needs and increasing number of cars, coal and fuel combustion PM and sulfur dioxide (SO₂) have spiked to record levels in recent years (Watts, 2005). This has left major metropolitan areas in China such as Beijing and Shanghai among the cities with highest levels of air pollutants globally (Kan, Chen, & Tong, 2012). Similarly, air pollution exposure is more severe than ever in India with sources ranging from traffic and industry to residential biomass burning and open burning of solid waste (Saraswat et al., 2013).

It is important to note that the first line of intervention to reduce air pollution exposure at a population level should be focused on reducing emissions at source as described above. Meanwhile, the effort should be continued to better understand the potential effects of air pollution on different body systems including the cardiovascular system. One of the more innovative methods to evaluate the health effects of higher air pollution exposure is the use of high efficiency particulate air
(HEPA) filtration to introduce an exposure concentration gradient while evaluating health outcomes, which will be discussed extensively in the following sections.

It has been shown that HEPA filters can remove a great portion of respirable particles (99.97% of 0.3 µm particles) (Yamada et al., 1984) and can reduce indoor PM concentrations by over 50%, which is significant considering the fact that people generally spend the majority of their time indoors (Batterman et al., 2011). It is important to note that unlike other air cleaners such as electrostatic precipitators and ion generators, HEPA filtration devices do not emit ozone particles, which are a health concern (Waring, Siegel, & Corsi, 2008). In addition, HEPA filters do not have any effect on other gases such as nitrogen oxides thus focusing the intervention on PM only.

An additional benefit of using HEPA filtration is that it might be beneficial in reducing individual-level PM exposure and potentially, alleviating adverse health effects. To evaluate the health effects of exposure to air pollution and to characterize the effectiveness of such individual-level interventions, there is a need for further research.

1.1 Literature Review

1.1.1 Components of Air Pollution

There are six common air pollutants, which are commonly known as “criteria pollutants”; these include ozone, PM, carbon monoxide (CO), nitrogen oxides (NOx), SO2, and lead. There have been a number of studies evaluating the relationship between these pollutants and health. There is some evidence linking sulfur dioxide, nitrogen dioxide, and CO exposure to adverse cardiopulmonary health outcomes; however, there is still uncertainty surrounding these relationships (Health Effects Institute, 2010a; Koken et al., 2003; Tarlo et al., 2001; Tsai, Goggins, Chiu, & Yang, 2003). There is also extensive evidence linking ozone exposure to adverse respiratory symptoms and mortality from respiratory causes (Ito, De Leon, &
More recent literature indicates that fine PM plays a major role in the development of adverse health effects in a range of body systems (e.g. cardiovascular and potentially reproductive) (Pope & Dockery, 2006). With increasing robust indications of the effects of PM on health, this study focuses on PM as the air pollutant of interest and its potential effects on endothelial function and systematic inflammation.

1.1.2 Physical and Chemical Composition of PM

PM is mixture of solid and liquid particles with a variety of physical and chemical characteristics. Particles are categorized based on aerodynamic diameter, which can be related to their deposition patterns, sources, and composition (Chow, 1995). In general, particles are divided into those with aerodynamic diameters of: 1. Between 2.5 μm and 10 μm (Coarse), 2. Less than or equal to 2.5 μm (Fine or PM$_{2.5}$), and 3. Less than 0.1 μm (Ultrafine). These categories are significant in that the smaller the aerodynamic diameter, the larger the surface area per mass, which could increase lung’s exposure to various compounds such as transition metals and free radicals.

Coarse particles are emitted into our environment in various ways including the suspension of dust and soil and through mining and farming, as well as the airborne release of pollen and mold. Fine particles are mostly formed by fuel combustion, wood and coal burning, and industrial processes. Similarly, ultrafine particles are formed from sources of combustion, their coagulation to form fine particles, and atmospheric reactions (Pope & Dockery, 2006).

Even in the same size categories, PM particles differ in morphology, surface charge, and most importantly chemical composition based on their source, making the study of their potential health effects based on their physicochemical characteristics very challenging (Schwarze et al., 2006). These characteristics can affect where particles will be deposited and what effects may result; morphology and surface charge, among other factors, can determine if the particles can penetrate into the air.
exchange region of the lungs, which makes their clearance more difficult while chemical composition (e.g. presence of transition metals) can have an effect on the level of toxicity. Very few studies have specifically compared the physicochemical characteristics of traffic-related PM and woodsmoke (WS) as two main sources of combustion-derived PM. The available literature reports some differences in polyaromatic hydrocarbon composition, particle size distribution, and elemental composition variation between these two sources (Hedberg et al., 2002). These findings might have implications for potential differences in the adverse health effects (e.g. systemic inflammation) caused by different sources of PM.

1.1.3 PM Exposure Health Effects

Indoor and outdoor air pollution is one of the main contributors to the global burden of disease (Pope & Dockery, 2006). Among the different components of air pollution, PM is unique in the sense that numerous studies have demonstrated well-defined and robust impacts on a multitude of body systems. There is also strong toxicological evidence linking PM from different sources to adverse health effects. While there are different sources of combustion-derived PM (e.g. traffic and WS), not all of them have been studied sufficiently to evaluate related health effects. As discussed in the following sections, currently there are strong suggestions of a link between exposure to traffic PM and different health outcomes (including cardiovascular health outcomes); however, other combustion sources have not been studied as extensively or compared to health effects involved with traffic PM exposure.

Numerous studies have investigated the potential adverse health effects of exposure to PM around the world. The early research on air pollution and its health effects predominantly focused on mortality and adverse respiratory health outcomes. In the past few decades, the focus has shifted towards other outcomes such as cardiovascular, reproductive, and cognitive effects. Previous studies have reported links between PM and morbidity and mortality attributed to short-term PM exposure (Crouse et al., 2012; Dominici F, Peng RD, Bell ML, & et al, 2006; Kloog,
Ridgway, Koutrakis, Coull, & Schwartz, 2013) or long-term PM exposure (Dockery et al., 1993; Pope et al., 1995; Pope et al., 2004). Furthermore, there have been reports of health effects from long-term exposure to relatively low concentrations of ambient PM including the Harvard Six Cities and American Cancer Society (ACS) studies. In a recent large cohort study in Canada, researchers found an elevated risk of death from non-accidental and cardiovascular causes at PM levels significantly lower than those in the Harvard Six Cities and ACS studies (Crouse et al., 2012). Studies of this sort further support the hypothesis that no threshold exists for PM exposures in the development of adverse health outcomes (Pope & Dockery, 2006).

It is important to note that different sources of PM could potentially result in different morbidity and mortality outcomes. Recent research has shown that combustion-derived fine PM exposure is one of the most detrimental components of air pollution (Kelly & Fussell, 2012). More specifically, some studies have identified PM$_{2.5}$ to have significantly greater effects on human health compared to larger particles potentially due to the fact that they can penetrate deeper into the lungs (Burnett et al., 2000; Cifuentes, Vega, Köpfer, & Lave, 2000; Schwartz, Dockery, & Neas, 1996). However, this is not to undermine numerous studies that have reported morbidity and mortality with exposure to coarse particles (Brunekreef & Forsberg, 2005).

1.1.3.1 PM Exposure and Mortality

Annually, 3.2 million premature deaths are attributable to ambient PM exposure around the world; PM also accounts for 3.1% of global disability-adjusted life years (DALYs) (Lim et al., 2012). It has also been estimated that exposure to solid fuels air pollutions is accounts for 3.5 million premature deaths and 4.5% of the global DALYs in 2010. In Canada, it is estimated that over 21,000 premature deaths are attributable to air pollution each year, which is 9 times greater than the number of deaths from traffic accidents (Canadian Medical Association, 2008).
Exposure to PM has been linked with reduced life expectancy and increased mortality. In a study conducted in the United States, Pope et al. (2009) found that a decrease of 10 µg per cubic meter (µg/m³) in the concentration of fine PM was associated with an increase of 0.61 year in life expectancy. They concluded that reductions in fine PM could lead to significant improvements in life expectancy (Pope, Ezzati, & Dockery, 2009).

In a landmark study, the association between air pollution with mortality was investigated in six U.S. cities (Dockery et al., 1993). As a prospective cohort study, 8,000 adults were followed for 14 to 16 years, linking mortality to different levels of air pollution in various cities. The authors found mortality rates to be 26% higher in the most polluted cities compared to the least polluted one (approximately 19 µg/m³ difference in PM\textsubscript{2.5} concentrations). Furthermore, mortality was most associated with fine PM air pollution exposure compared to total particle concentration.

In an extension of the “U.S. six cities” study, Laden et al. (2000) directly investigated the association of traffic combustion-derived PM\textsubscript{2.5} and change in mortality rates. The results indicated a 3.4% increase in daily mortality per 10 µg/m³ increase in mobile combustion source PM\textsubscript{2.5} levels. They concluded that fine particulates from mobile combustion sources were significantly associated with increased mortality (Laden, Neas, Dockery, & Schwartz, 2000).

In a more recent cohort study in Canada, Crouse et al. (2012) looked at 2.1 million individuals between 1991 and 2001 and identified the deaths occurring during this period. After assigning PM\textsubscript{2.5} concentrations using ground-base station data, they found significant increases in nonaccidental and cardiovascular mortality with hazard ratios of 1.15 (95% CI, 1.13, 1.16) and 1.31 (95% CI, 1.27, 1.35), respectively. Their results are similar in magnitude to those of the ACS study where over 550,000 individuals were followed for 7 years and the authors found significant increase in all-cause, cardiopulmonary, and cancer mortality (Pope et al., 1995).
1.1.3.2 PM Exposure and Morbidity

Along with mortality studies, numerous studies have evaluated the morbidity related to exposure to PM air pollution. With the growing body of literature, we are gaining more insight into the diverse health impacts associated with exposure to PM. Exposure to PM has been associated with various effects on physiological functions and subclinical symptoms, a range of cardiovascular conditions (e.g. myocardial infarction and cardiac arrhythmia) (Dockery, 2001), exacerbation of asthma (Anderson, Favarato, & Atkinson, 2013), chronic obstructive pulmonary disease (Ko & Hui, 2012), stroke (Mateen & Brook, 2011), lung cancer (Raaschou-Nielsen et al., 2010, 2011), and premature births (Brauer et al., 2008). Moreover, the International Agency for Research on Cancer (IARC) recently classified outdoor air pollution and PM as known human carcinogens (IARC Group 1) due to the link between exposure to PM and increased risk of lung cancer (Loomis et al., 2013).

1.1.3.2.1 Air Pollution and Cardiovascular Health

Numerous studies have successfully linked exposure to air pollution to adverse cardiovascular outcomes and mortality. Kunzli et al. (2010) evaluated the potential cardiovascular effects of living in close proximity to traffic; they concluded that individuals living within 100 meters of a freeway have a rate of atherosclerosis progression twice that of the general population (Künzli et al., 2010). There is an increasing body of evidence linking long-term exposure to higher levels of PM and the progression of atherosclerosis, however, there is still no conclusive evidence on the relationship (Brook et al., 2010).

There have been a number of Canadian studies demonstrating associations with cardiovascular outcomes; in a cohort of over 452,000 individuals, proximity to major roads was linked to an increase in coronary heart disease (CHD) mortality (Gan et al., 2011). In a separate study, Gan et al (2010) found that moving away from high traffic roads and freeways reduced the risk of CHD mortality (Gan et al., 2010). Moreover, several other studies have reported a link between traffic-related air
pollution (TRAP) exposure and hypertension and stroke (Baccarelli et al., 2009; Fuks et al., 2011). There is also evidence reporting associations between TRAP exposure and myocardial infarction (von Klot et al., 2011). Finally, a review of the literature on TRAP and cardiovascular health by the American Heart Association concluded that there seems to be an association between TRAP and adverse cardiovascular event risk, however, there is still a significant need for more research to identify potential links (Brook et al., 2010).

Despite being a major source of particulate air pollution, limited data is available on the toxicity of residential wood combustion (RWC) PM, leading to the false impression that RWC is not an important source of toxicity compared to TRAP (Kocbach Bølling et al., 2009; Naeher et al., 2007). The IARC has classified indoor emissions from household combustion of biomass (primarily wood) as a group 2A carcinogen (i.e. probably carcinogenic to humans) (International Agency for Research on Cancer, 2012). There has been some evidence that the potential adverse health effects as a result of WS exposure in developed countries is not significantly different than for ambient particles from other sources (Boman, Forsberg, & Järvholm, 2003; Naeher et al., 2007). Adding to the complexity of investigating WS PM is the fact that emission characteristics depend on both the fuel and burn conditions (Guillén & Ibargoitia, 1999). With regards to the respiratory effects due to WS particles, Naeher et al. (2007) point out that at the present time, there is insufficient evidence indicating that WS particles have less effect than other major categories of combustion derived particles of the same size range. Various studies have linked exposure to WS PM with respiratory health outcomes including respiratory symptoms in children (Browning, Koenig, Checkoway, Larson, & Pierson, 1990), decreases in lung function in asthmatic children (Allen et al., 2008; Koenig et al., 1993) and adults with COPD (Trenga et al., 2006), and increased asthma emergency room visits (Schwartz, Slater, Larson, Pierson, & Koenig, 1993; Sheppard, Levy, Norris, Larson, & Koenig, 1999). Moreover, there is evidence of an association with low birth weight (Gehring, Tamburic, Sbihi, Davies, & Brauer,
2014), otitis media (MacIntyre et al., 2011), and COPD hospitalizations (Gan, FitzGerald, Carlsten, Sadatsafavi, & Brauer, 2013).

However, we still lack the necessary evidence to comment on the potential adverse health effects of WS particles on the cardiovascular system and cancer (Naeher et al., 2007). There have been suggestions of a potential link between WS exposure and cardiovascular morbidity and mortality. A study conducted in a predominantly WS affected city in Australia investigated the relationship between exposure to WS PM and cardio-respiratory illness hospital admissions. The researchers found significant increases in hospital admissions with increases in WS PM (McGowan, Hider, Chacko, & Town, 2002). In another study conducted in one of the most highly WS polluted cities in the world in Peru, the authors observed significant associations between ambient PM levels and hospital admissions and cardiovascular mortality (Sanhueza et al., 2009).

Based on the available literature, there is a potential for combustion related air pollution to be responsible for adverse cardiovascular health outcomes in the general population. With current knowledge gap in this topic, there is a need for more research on the effects of exposure to WS PM and cardiovascular health.

1.2 Mechanisms of Action

The human lung has a surface area of 40-120 m², which is exposed to 10-20,000 L of ambient air every day. The lung employs various defense mechanisms to deal with the particles that deposit on its surface, which include mechanical removal and biochemical neutralization of harmful particles. Mucociliary clearance mechanisms remove the larger particles that have deposited in regions such as the trachea and bronchi into the throat, which can then be swallowed. However, smaller particles can penetrate to the lower airways and into the oxygen exchange region of the lungs; they are then engulfed by macrophages, which are either removed by the phagocytosed particles through mucociliary clearance system or are passed through
the alveolar wall into the lymphatic vessels. The defense mechanisms of the lung may be overwhelmed by the toxicity of the particles and particle number overload (Salvi & Holgate, 2001). It has been shown that smaller particles of a diameter of 2.5 µm are not cleared effectively and remain in the lungs to a greater extent (77% retention rate) compared to particles of 8.2 µm (15% retention rate) after 24 hours (Svartengren, Linnman, Philipson, & Camner, 1987). Moreover, with the small size of the PM_{2.5}, these particles will have a greater surface area increasing the area available for the adsorption of toxic compounds. The size and surface area of fine particles could provide an opportunity for the particles to impact the lungs and the whole body (Kelly & Fussell, 2012).

Another proposed mechanism indicates that with increased particle presence in the airways, the phagocytic capacity decreases which leads to PM presence in the lungs for an extended time and hence, increase the interaction with various cell types such as epithelial cells (MacNee, Li, Gilmour, & Donaldson, 1997). Particles containing transition metals and the free radicals produced by them can lead to oxidative damage and macrophage activation in the lungs. This could lead to acute cellular and mediator inflammatory response in the airways through the release of pro-inflammatory mediators. Moreover, the epithelial cells phagocytose fine PM upon contact leading to an increase in the production and release of pro-inflammatory cytokines, strengthening the inflammatory response.

Brook et al. (2009) propose another plausible mechanism for the cardiovascular health outcomes of exposure to PM_{2.5}. According to their hypothesis, inhaled PM_{2.5} interacts with pulmonary irritant receptors lining human airways; this could result in impacts via the autonomic nervous system leading to prohypertensive response and cardiovascular symptoms such as variations in heart rate and blood pressure (Brook et al., 2009).

A third hypothesized mechanism of action of fine PM is through penetration into the interstitium. After entering the interstitium, inflammatory mediators are released
which can result in a low-grade systemic inflammatory response affecting blood platelets and clotting factors. This could potentially lead to adverse cardiovascular effects, especially in those with pre-existing cardiovascular conditions (Salvi & Holgate, 2001). For this mechanism, it has been hypothesized that oxidative stress links PM exposure to inflammation, endothelial dysfunction, and atherosclerosis (Brook et al., 2010). TRAP particles contain transition metals, which in turn produce hydroxyl radical that can cause oxidative stress and inflammation (Ghio, Stonehuerner, Dailey, & Carter, 1999; Valavanidis, Vlahyionni, & Fiotakis, 2005).

### 1.3 Two Major Sources of Combustion-Derived PM

There is evidence of both combustion and non-combustion emission sources contributing to ambient PM$_{2.5}$ in our cities. The major sources of combustion derived PM vary in different parts of the world. For example, in China, coal combustion, dust, biomass aerosol, and car exhaust are the main contributors of PM$_{2.5}$ with coal combustion being the greatest emission source (Meng et al., 2007; H. Wang et al., 2008; Xinhua Wang, Bi, Sheng, & Fu, 2006; Zheng, Salmon, Schauer, Zeng, & Kian, 2005). In fact, in many parts of the developing world it is the combustion of coal and biomass that contribute extensively to suspended PM$_{2.5}$. In North America, the situation is different, with traffic-related and wood combustion being two of the major sources of combustion-derived PM. Wood combustion PM emissions increase moving north in North America (Maykut, Lewtas, Kim, & Larson, 2003; Zheng et al., 2005). For the purposes of this study, the focus will be on the two predominant sources of combustion derived PM$_{2.5}$ in North America: Traffic-related PM and WS PM.

#### 1.3.1 Traffic-Related PM

More and more scientific evidence is linking PM$_{2.5}$ exposure from combustion sources, which include traffic, industries and domestic heating and cooking, to adverse cardiovascular outcomes (Goldberg et al., 2001; Han & Naeher, 2006). Traffic-generated emissions are one of the major sources of exposure to PM. In Metro Vancouver, TRAP accounts for approximately 12% of the total PM emissions
in the region (Metro Vancouver, 2010). Furthermore, approximately 90% of the PM associated with motor vehicles is in the PM$_{2.5}$ size range increasing the possibility of deeper penetration into the lungs (Health Effects Institute, 2010a). It has been estimated that approximately 30-45% of typical urban populations in North America live in close proximity to highway or major road (Health Effects Institute, 2010a). Estimates in Canada indicate that about 32% of the Canadian population lives in areas of high exposure to TRAP (Brauer, Reynolds, & Hystad, 2012; Health Effects Institute, 2010b). Furthermore, the United Nations has estimated that approximately 600 million people in urban areas worldwide are exposed to dangerous levels of traffic-generated air pollutants (Cacciola, Sarvà, & Polosa, 2002). With such a great proportion of the population exposed to air pollution and considering the overwhelming evidence on potential health effects, TRAP is an important public health issue.

1.3.2 WS PM

Based on the available estimates, over half of the world’s households use solid fuel every day. Approximately 95% of this consists of wood and agricultural residues. In spite of its more prevalent use in developing countries, residential wood combustion (RWC) is also impacting air quality in Canada. RWC is a major source of PM emissions in higher latitudes accounting for over 25% of fine PM emissions in Canada (Andrea Careless, 2004; Barregard et al., 2006b; Swiston et al., 2008). In Metro Vancouver, WS accounts for 25% of PM$_{2.5}$ emissions in the region (Metro Vancouver, 2013). With the rising costs of other fuel options and having wood as a cheaper and readily available alternative, the significance of RWC emissions is expected to increase in the future (deB. Richter et al., 2009; Zezima, 2008). The available data on RWC indicate that WS is not exclusively an issue in the developing world; the use of wood and other biomass increased at an annual rate of 2.4% during the 1990s in North America (Naeher et al., 2007).
Despite the increasing contributions of WS PM to the general air pollution, there have been very few studies comparing the health effects of TRAP with WS air pollution, leaving a wide knowledge gap for future policymaking. This is primarily due to the fact that many pollutants are shared between various sources. In most cases, it is difficult to directly determine the degree to which residential WS contributes to indoor and outdoor particle exposure (Kocbach Bølling et al., 2009).

1.4 Surrogates of TRAP and WS PM

1.4.1 Hopanes

Hopanes are specific compounds contained mainly in the hydrocarbon fractions of petroleum products and are relatively stable in the ambient environment. The presence of hopane biomarkers in aerosols indicates a fossil fuel source (e.g. gasoline and diesel) (Simoneit, 1999). Being specific to fossil fuels and oils, these tracers can be used as indicators of primary particle emissions from diesel and gasoline engines (Cass, 1998). Schauer et al. demonstrated and validated that hopanes can be used as organic tracers for vehicle emissions exclusively (Rogge, Hildemann, Mazurek, Cass, & Simoneit, 1993). Hopanes have also been used in some validated source apportionment studies further indicating their relevance to TRAP (Lin, Lee, & Eatough, 2010). There has also been some evidence on the similarity of hopane and TRAP PM relationship with distance from major roads and highways (Olson & McDow, 2009). The authors measured the concentration of hopanes at varying distances from a highway and found that hopanes concentration was greater closer to the highway and decreased moving away, as one would expect with TRAP PM concentrations. Another study in Texas identified the same relationship with decreasing hopanes concentration with increasing downwind distance from highway. Considering the available evidence, hopanes can be considered suitable organic markers for characterizing the proportion of TRAP in indoor PM$_{2.5}$ concentrations.
1.4.2 Optical Absorbance

In the current study, optical absorbance was measured to represent elemental carbon (EC), which is a component of traffic combustion emissions. As surrogates of combustion derived PM, studies have shown a high correlation between EC and absorbance (Janssen et al., 2000; Kinney, Aggarwal, Northridge, Janssen, & Shepard, 2000). Various studies have also found an association between exposure to EC and morbidity and mortality in the general population and different vulnerable sub-populations (Fang et al., 2012; Geng et al., 2013; Janssen et al., 2011; Nichols, Owens, Dutton, & Luben, 2013; Xi Wang et al., 2013). Moreover, there are some suggestions that EC may be a more sensitive indicator of traffic-related impacts on air quality compared to PM mass (Keuken, Jonkers, Zandveld, Voogt, & Elshout van den, 2012).

1.4.3 Levoglucosan (LG)

Cellulose is one of the main polymers found in wood (50%-70% by weight) (Simoneit, 1999). LG is a by-product of cellulose combustion, which is specific to combustion of biomass. It is a favorable organic tracer for WS since it is highly stable in the environment (Fraser & Lakshmanan, 2000). It has also been used in various studies of WS exposure in humans (Allen et al., 2008; Allen, Leckie, Millar, & Brauer, 2009; Naehler et al., 2007). The significance of this organic marker is that it enables us to determine the extent of WS influence on indoor PM$_{2.5}$ concentrations.

1.5 Study Rationale

Considering the available evidence on the causal relationship between air pollution and morbidity and mortality, we need to evaluate potential interventions, which can be used to minimize exposure and associated health risks (van Erp et al., 2008). Among various adverse health effects related to exposure to air pollution, CVD has a major population health impact. Despite various efforts to identify the sources of PM responsible for cardiovascular health effects, there is still a knowledge gap in the literature. Moreover, no studies have directly compared two sources of PM and their
potential differential effects on cardiovascular health, which further demonstrates the need for studies of this kind with regards to CVD.

A variety of successful interventions have been used during the past few decades to reduce TRAP and RWC PM emissions and exposures. With regards to TRAP, there have been efforts to change individual behavior, improvements to combustion technology, fuel standards, more stringent emission requirements, and land-use planning and transportation management aimed to decrease exposure and potential health impacts (Brauer et al., 2012; Giles et al., 2011). Examples of such interventions include London’s congestion charge scheme restricting the number of vehicles entering central London daily, which resulted in a reduction in air pollution and mortality (Tonne, Beevers, Armstrong, Kelly, & Wilkinson, 2008). As the other major source of combustion-derived PM$_{2.5}$ emissions, there have been efforts to identify interventions to reduce exposure to WS PM. One of the effective measures has been the implementation of woodstove exchange programs to replace old, inefficient stoves with cleaner burning new stoves. A successful wood stove exchange program was implemented in Libby, Montana which resulted in the replacement of over 90% of non-certified stoves; A reduction of 20% was witnessed in ambient fine PM concentrations while the levels of LG decreased by 50% (Bergauff, Ward, Noonan, & Palmer, 2009). In a study conducted in Tasmania, Australia, wood heaters were gradually replaced with electrical heating, reducing the prevalence of woodstove use from 66% to 30% in all households (Johnston, Hanigan, Henderson, & Morgan, 2013). This intervention resulted in a 40% drop in PM$_{10}$ levels and over 11% decrease in all-cause mortality among males. The discussed examples illustrate the benefits that targeted interventions can have on traffic and WS air pollution and related adverse health outcomes.

Household-level exposure interventions can also prove to be effective with regards to reducing air pollution exposures and health risks. Portable HEPA filters appear to be a viable approach to reduce indoor respirable particle concentrations (Barn et al., 2008; Sublett et al., 2010; Yamada, Miyamoto, Mori, & Koizumi, 1984). Some
research evidence suggests that HEPA filters can significantly reduce PM exposure in subjects exposed to high TRAP (Bräuner, Forchhammer, et al., 2008). HEPA filters can be considered a practical intervention for reducing PM exposure since they can be used to impact the most susceptible populations exposed to high levels of air pollution within a community. In addition, they are relatively inexpensive to purchase and maintain, making them accessible for the general population and potentially low-income households through inexpensive subsidies (Fisk, Faulkner, Palonen, & Seppanen, 2002).

Most previous research on HEPA filter interventions has focused on indoor aeroallergens and asthma aggravation (Ezzati & Kammen, 2002). In a recent systematic review of the available literature, Fisk (2013) looked at 9 HEPA filtration intervention studies and their effects on allergy and asthma symptoms. Based on this review, there were significant measurable drops in aeroallergens with filtration. The author concluded that there is persuasive evidence suggesting that filtration systems might be modestly effective in reducing adverse health symptoms among those with allergies and asthma, especially in the presence of large allergen sources. It should be noted that only a small proportion of these studies reported statistically significant improvements in health outcomes, with most being small to moderate in magnitude. Despite having multiple studies evaluating the effect of HEPA filtration on allergies and asthma, there have been very few studies investigating the effectiveness of HEPA filter for improving cardiovascular health.

Current available evidence indicates that HEPA filtration inside participants’ residences could improve microvascular endothelial function and decrease systemic inflammation. In a HEPA filter intervention study in Denmark, Brauner et al. (2008) reported improvements in endothelial function after reductions in TRAP PM with indoor filtration. In a similar study, Allen et al. (2011) used HEPA filtration as an intervention in a WS impacted community in Canada, and found improvements in both endothelial function and marker of CVD risk (C-reactive protein (CRP)) after reductions in WS PM with indoor filtration. The similar-sized effects among TRAP-
and WS-exposed individuals was the initial source of motivation for the current study to evaluate TRAP and WS PM in the same study.

Furthermore, it has been shown that particles containing transition metals and the free radicals produced by them can lead to oxidative damage and macrophage activation in the lungs. This could result in acute cellular and mediator inflammatory response in the airways through the release of pro-inflammatory mediators. Some of these particles can penetrate through into the interstitium. After entering the interstitium, inflammatory mediators are released which can result in a low-grade systemic inflammatory response, which could lead to adverse cardiovascular effects (Salvi & Holgate, 2001). There appears to be more transition metals in TRAP PM compared to WS PM, which can generate hydroxyl radicals and lead to oxidative stress (Ghio et al., 1999; Verma et al., 2009). This chain of reactions is considered as one of the pathways that links PM exposure with inflammation (Brook et al., 2010).

In addition, there has been some evidence indicative of differential depositional patterns between TRAP and WS PM in lungs. Two recent human experimental studies concluded that the respiratory tract deposition of traffic particles was 16 times higher than residential WS particles in addition to a total surface area 3 times that of WS particles (Löndahl et al., 2008; Löndahl et al., 2009); there is also in vitro evidence that traffic particles can have a greater inflammatory effect on the lungs (Kocbach, Herseth, Låg, Refsnes, & Schwarze, 2008). These studies support the potential for differential effects of TRAP and WS PM on health and the need for a comparison between these two sources of combustion-derived PM.

Although there are a number of studies that have evaluated the relationship between TRAP or WS PM and various health effects, it is very difficult to directly compare their conclusions. Different studies differ in their exposure/outcome assessment methodologies and statistical analysis, hence differences in effect estimates between TRAP and WS exposed could be due to more or less
misclassification error for either of the sources. To further complicate comparisons, the size of exposure gradients differ in different studies making it very difficult to directly compare the results. By evaluating both TRAP and WS in the same study, this study addressed the first issue by utilizing detailed in-home exposure measurements for both groups. As for the second obstacle, HEPA filtration devices were used to produce an exposure gradient of similar magnitude in both groups.

Overall, this study aims to help identify the most important sources and components of air pollution mixture relevant to cardiovascular health and to assist policy-making bodies target the key components to more effectively protect public health. Considering this overarching rationale, this study aims to determine the potential difference in subclinical cardiovascular health effects between WS- and TRAP-related particulate exposures, using HEPA filtration to generate a PM$_{2.5}$ concentration gradient, and to evaluate the use of HEPA filters as an intervention for TRAP and WS PM concentration reduction.

1.6 Objectives and Hypotheses

In order to evaluate the cardiovascular health risks of RWC and TRAP-generated PM and the health benefits of HEPA filters as an intervention, a randomized single-blind crossover study was designed with the following objectives:

a) To evaluate the effectiveness of HEPA filters in reducing indoor PM in areas where TRAP and RWC are important sources

b) To quantify the relationship between exposures to RWC- and TRAP-derived PM air pollution and subclinical indicators of cardiovascular disease (CVD) risk including endothelial function and high sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), and band cell counts (BCC) as indicators of systematic inflammation;
c) To compare the relative impact of HEPA filtration for TRAP and RWC PM sources on microvascular endothelial function and hs-CRP, IL-6, and BCC as indicators of systemic inflammation among healthy adult participants.

In this study, we hypothesize that:

a) The use of indoor HEPA filtration for seven days will result in reductions in indoor concentrations of PM$_{2.5}$ compared to seven days of no filtration.

b) A reduction in combustion PM$_{2.5}$ exposure in healthy adults by implementing indoor HEPA filtration will lead to decreases in hs-CRP, IL-6, and BCC and improvements in microvascular function.

c) There will be a greater impact on the two outcomes of interest (measures of systemic inflammation and microvascular endothelial dysfunction) among those living in TRAP-impacted locations than among those living in WS-impacted locations.

The proposed hypotheses are supported by the available literature on the effectiveness of HEPA filters in reducing indoor PM levels (Allen et al., 2011; Barn et al., 2008; Batterman et al., 2011; Bräuner, Møller, et al., 2008; Weichenthal et al., 2013) and the potential for the greater toxicity of TRAP PM compared to WS PM (Kocbach et al., 2008; Löndahl et al., 2008; Löndahl et al., 2009).
2 Methods

2.1 Study Design

This study had a single-blind randomized crossover design where participants were blind to the status of HEPA filtration. It should be noted that the laboratory technicians performing blood analysis were blinded to the HEPA filter status as well. HEPA filters were used as an intervention to reduce PM$_{2.5}$ exposure and produce an exposure gradient for the duration of the study. For this study, we aimed to recruit a total of 100 participants, 50 from each exposure category (i.e. TRAP or WS). Individuals were recruited from homes in high TRAP or high RWC in Metro Vancouver, which were identified using previously developed air pollution spatial models for the region.

Each home was monitored during two consecutive weeks for a total of 14 days with one HEPA filtration device in the living room and one in the main bedroom. During one 7-day period the HEPA units were operated with a HEPA filter in them and during the other 7-day period there was no HEPA filter in the unit (i.e. placebo filtration). As illustrated in Fig. 2-1, each home was randomly assigned to one of the two possible orders of HEPA/no HEPA by coin flip on the first day of sampling: one group where there was HEPA filtration in effect during the first week and no HEPA in the second week, or the other group where there was no HEPA filtration during the first week and HEPA filtration in the second week. In each home, there were between 1 to 3 participants being evaluated at the same time.
Air pollution concentrations were measured both indoors and outdoors in addition to the study subjects’ time-location patterns for the full duration of the study (i.e. two seven-day samples). Furthermore, biological indicators of endothelial function, as the primary outcome variable of this study, and systemic inflammation were assessed after each of the 7-day periods, in addition to baseline for systematic inflammation. The data from these assessments was used to compare each individual’s assessment between filtration and placebo sessions.

2.2 TRAP and WS Region Selection in Greater Vancouver

In order to accurately categorize postal codes into either high TRAP/low WS or low TRAP/high WS, we needed to identify such regions in Greater Vancouver Region. Spatial models of TRAP have been previously developed for several traffic-related air pollutants in greater Vancouver (Henderson, Beckerman, Jerrett, & Brauer, 2007). Henderson et al. (2007) used measurements of NOx and light absorbing carbon at 116 and 25 locations, respectively, in two seasons to develop TRAP land use regression models for Metro Vancouver. Larson et al. (2007) developed a spatial model for WS dividing the region into three tertiles of WS concentrations during hypothesized highest emission periods. They used nighttime PM$_{2.5}$ mobile monitoring in winter and a two-week average PM$_{2.5}$ and LG concentration measurements to develop land use regression models for WS in Metro Vancouver.
Using these two spatial models enabled the identification of regions and populations with exposure levels of interest and minimized exposure miscategorization (Fig. 2-1).

Figure 2-2 a. modeled TRAP concentrations (Henderson et al., 2007); b. modeled WS tertiles (Larson et al., 2007); c. high TRAP and low WS postal codes; d. high WS and low TRAP postal codes

For the purposes of this study, “traffic area” was defined as regions with an annual average NO concentration of >50 ppb and WS concentration in the bottom tertile. The areas meeting these criteria included 730 postal codes and approximately 13,000 residents. The “WS area” was defined as regions with an annual NO average of <15 ppb and WS concentration in the top tertile. The WS area included 800 postal codes and approximately 23,000 residents. The extracted postal codes from these two models were then used to mail out informational letters to recruit participants.
2.2.1 Home Categorization Verification

In order to further verify traffic and WS home categorization that were used to recruit participants, some additional analysis was performed. Using ArcGIS Desktop 10 (ESRI, Redlands, CA: Environmental Systems Research Institute) and maps provided by DMTI Spatial Inc. (Markham, Ontario, Canada), the distance of individual homes to major roads or highways were extracted. In addition, highway or major road length at varying buffers was calculated. In general, it was expected that TRAP homes be closer to major road or highway with a greater length of such roads in their immediate vicinity compared to WS homes.

2.3 Participant Recruitment Campaign

In order to recruit participants, invitation letters with study information and contact information were mailed to postal codes that were identified using TRAP and WS models described earlier (Appendix I). Subjects were then recruited after a telephone interview (Appendix II) and based on our inclusion criteria. In addition, written informed consent was obtained from each participant prior to starting data collection (Appendix III). An honorarium of $250 was offered to each participant who completed the study. In addition, participants were promised to be sent all the results for exposure and biological measurements at the end of the study (Appendix IV).

2.4 Study Participant Characteristics

The basic inclusion criteria of this study were to recruit individuals over 19 years old, non-smokers, and those living in the target areas. To minimize occupational exposure and maximize the exposure reduction potential of the HEPA filters, participant priority was given to those who did not work or volunteer outside the home. In order to meet the study requirement of recruiting healthy adults and having a homogenous study population, a number of exclusion criteria were followed.
Individuals were excluded if they had any condition that might affect exposure, cardiovascular health outcomes, and/or microvascular endothelial function. Subjects with recent surgeries, diabetes, heart disease, hypertension, metabolic syndrome, asthma, and COPD in addition to pregnant women were excluded as these conditions might have an effect on systemic inflammation. Moreover, due to the fact that we measured endothelial function using probes on fingertips (explained in more detail in the following sections), individuals with Reynaud’s syndrome were excluded as this condition might interfere with accurate measurements and was excluded. In addition, those in occupations with high exposures to air pollution such as bus drivers and mechanics were excluded. Finally, individuals taking anti-inflammatory medications were also excluded.

The goal of this study was to recruit a homogenous population of healthy adults. Moreover, despite having some of the highest TRAP concentrations of the greater Vancouver region in Downtown Vancouver, this area was excluded from the study since most residences are in high-rise buildings. There is some evidence that indicates ground-level exposure might not be well correlated with levels determined in high-rise buildings due to vertical concentration gradients (Restrepo et al., 2004; Villena et al., 2011). Based on the same evidence, residences above the third floor were also excluded.

2.5 Participant Preparation Before Sampling

At the beginning of each sampling session, the sampling plan was explained to the residents in detail by both the environmental and the health technician. The environmental technician explained the devices being placed in the home and discussed the location of sampling equipment with the participants. The health technician reviewed the consent form with the participants and obtained their signature. Afterwards, the dwelling information form was completed with participants (Appendix V). Furthermore, time-location-activity diaries were explained to the participants ensuring that they understand how they should be filled out on a daily basis for the duration of the study (Appendix VI). The study
protocol was approved by the ethics committee at Simon Fraser University (Appendix VI, File # 2011S0431).

2.6 **Study Period**

All exposure and health measurements were conducted between December 5\textsuperscript{th}, 2011 to August 21\textsuperscript{st}, 2012. WS homes were sampled from December to April while TRAP homes were sampled from December to August.

2.7 **HEPA Filtration**

One of the most important factors in maximizing the efficiency of HEPA filtration devices is choosing a device with sufficient filtered air delivery for the room size of interest. Hence, we used two different models of filtration devices suitable for areas they were placed in. In the bedroom, smaller devices (18150, Honeywell, Tennessee, US) were used, which are effective for rooms up to 197 square feet in size. For the main living room, larger devices (50250/50300, Honeywell, Tennessee, US) were operated, which are effective for rooms up to 390 square feet in size (Figure 2-3).

![HEPA Filtration Devices Used – Honeywell 50250/50300 (Left) & Honeywell 18150 (Right)](image)

In the current study, HEPA filtration devices were mainly used to introduce a concentration gradient of PM\textsubscript{2.5} between filtration and no filtration weeks. The concentration gradient was then used to characterize the potential change in health effects with a reduction in PM\textsubscript{2.5} exposure. In addition, we investigated the potential
difference in efficiency of HEPA filtration for removal of PM from two major sources of combustion-derived PM$_{2.5}$ (i.e. TRAP and WS).

2.7.1 *Electricity Use Meter*

An electricity meter (Kill A Watt P4400, P3 International, NY, USA) was installed between the HEPA filtration device and the power outlet. The purpose of this device was to assist with estimating the usage of the device during the study period. Prior to the study, each of the different filtration devices was operated for one week in a laboratory setting. The amount of electricity used was recorded for three output settings on each device (i.e. low, medium, and high). After each sampling session, the amount of electricity used was compared to previously estimated electricity usage at each setting. The homes had to meet at least the approximated electricity use at the low setting for each type of device to verify that filtration devices were used for the duration of this study.

2.8 *Health and Exposure Measures*

Various health and exposure measures were included in this study. At the beginning of each sampling session, the sampling plan was explained to the residents in detail by both the environmental and the health technician. Moreover, a health log was completed with the health technician's assistance at the end of each sampling week (Appendix VIII). Table 2-1 presents the health and exposure measures used, rationale for use, and measurement methods.
Table 2-1 Health and Exposure Measures

<table>
<thead>
<tr>
<th>Health Measure</th>
<th>Rationale</th>
<th>Measurement Method</th>
</tr>
</thead>
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<tr>
<td>RHI</td>
<td>Endothelial Function</td>
<td>EndoPAT</td>
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<tr>
<td>CRP</td>
<td>Systematic Inflammation</td>
<td>Immunoassay (Luminex 100)</td>
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<tr>
<td>IL-6</td>
<td>Systematic Inflammation</td>
<td>Immunoassay (Luminex 100)</td>
</tr>
<tr>
<td>Band Cell Counts</td>
<td>Systematic Inflammation</td>
<td>Manual Count</td>
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<table>
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<tr>
<th>Exposure Measures</th>
<th>Rationale</th>
<th>Measurement Method</th>
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</thead>
<tbody>
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<td>PM$_{2.5}$</td>
<td>Primary Exposure</td>
<td>Harvard Impactor/SKC Leland Legacy Pumps</td>
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<td>Hopanes</td>
<td>Traffic Marker</td>
<td>GC/Mass Spectroscopy</td>
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<tr>
<td>Levoglucosan</td>
<td>Woodsmoke Marker</td>
<td>GC/Mass Spectroscopy</td>
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<td>Indoor Temperature</td>
<td>Between- and within-participant comparisons</td>
<td>Continuous Data Logger</td>
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<tr>
<td>Activities</td>
<td>Potential exposure influence</td>
<td>Questionnaire</td>
</tr>
<tr>
<td>Time-Location Pattern</td>
<td>Potential exposure influence</td>
<td>Questionnaire</td>
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</table>

2.9 Exposure Measurements

2.9.1 PM$_{2.5}$

Gravimetric indoor and outdoor samples of PM$_{2.5}$ were collected for the duration of each 7-day session for all homes. Sampling was conducted using a Harvard Impactor (Air Diagnostics and Engineering Inc., Naples, Maine, USA) attached to a SKC Leland Legacy pump operated at a flow rate of 10 liter/minute. Each pump was calibrated using a BIOS DryCal Defender 520 (Mesa Laboratories Inc., Colorado, USA) at each sampling location after a five-minute warm up period and using the assembled sampling train with all components in place. In short, DryCal was attached to the Harvard Impactor with a calibration cap while the pump was running. If necessary, the pump’s flow rate was adjusted to reflect 10 liters/min on the calibrator.
Samples were collected on 37 mm 2µm pore size Pall Teflo membrane filters with ring. Each filter was placed in a filter cassette holder in a laboratory setting and then placed in a sealed petri dish for transport. The sampling train was assembled upon arrival in each home and a filter (in its cassette) was placed in the Harvard Impactor. After each seven-day sampling period and prior to removing the filter, post-flow of the pump was measured using BIOS DryCal Defender (Mesa Laboratories Inc., Colorado, USA) and its calibration cap. Finally, the filter was removed from the Harvard Impactor and secured in its respective petri dish. The petri dish was placed in a Ziploc bag and in a foam padded box for transport to the OEH laboratory at UBC (Allen, Karlen, & Nichol, 2014).

2.9.2 Indoor Set Up

All indoor equipment was placed in the living room where there would be minimal disruption to the residents and the sampling equipment. Due to the amount of noise produced by the sampling equipment and despite the fact that individuals spend more time in the bedroom, exposure measurements were conducted in the living room. Instruments were placed a meter away from walls, corners, windows, air conditioners, and any other ventilation outlet/inlets.

The HEPA filtration devices were also placed in areas of the living room and the main bedroom where there would be minimal interference and least direct air current to occupants. Moreover, special care was taken to maximize the distance between air sampling instruments and HEPA filtration devices. A detailed description of the indoor set up is included in the supplementary standard operating procedure (SOP) document (Study Protocol III) (Allen et al., 2014).

2.9.3 Gravimetric Analysis of the Filters

The filters were equilibrated for at least 48 hours in humidity and temperature controlled room (35±5% RH, 22±3°C) at the School of Population and Public Health (SPPH) Occupational and Environmental Health laboratory in the University of
British Columbia prior to measuring pre- and post-weights. After the equilibration period, a radioactive alpha emitter neutralizer (NRD LLC., Grand Island NY) was used for approximately 2 seconds to remove any potential static charge present. The filters were then weighed in triplicate using a Sartorius M3P microbalance (1 µg resolution, ± 2 µg sensitivity). Triplicate weights were required to be within 10 µg of each other otherwise the filters had to be reweighed until the criterion was met. The average of each triplicate was used as the final weight. Pre-weighed filters were placed in clean petri dishes, which were labeled with a letter followed by three digits (e.g. A100). All pre-weight filters were stored in the humidity and temperature controlled room and removed only when needed for sampling. After sampling, the filters were removed from Harvard Impactors and placed into their respective petri dishes, and equilibrated for at least 48 hours prior to weighing, following the same procedure as used for pre-weights (Allen et al., 2014).

2.9.3.1 Quality Control (QC) Filters

Prior to each filter weighting session, three previously weighed, unused filters were used as QC filters. The weight of each QC filter was then compared to previously developed mean, warning (mean ± 2SD), and control (mean ± 3SD) of all previous repeated weightings of the same filters. Upon verifying that all triplicate pre-weights of the QC filters are with the control limits, the gravimetric analysis of filters would commence (Allen et al., 2014).

2.9.3.2 Field and Lab Blanks

Field blanks were collected at the first home and then every second home visit after that (i.e. Home 1, 3, 5, etc.). Field blanks were prepared by inserting an unused filter into a filter cassette and then into a clean and assembled Harvard Impactor. The Harvard Impactor was closed without turning the sampling pump on. After waiting for approximately 30 seconds, the filter was removed from the Harvard Impactor and filter cassette and placed back into a labeled and clean petri dish. The field blank was treated as a regular sample filter after this point (Allen et al., 2014).
Mean weight of field blanks was deducted from all filter weights prior to performing further calculations. The same procedure was followed for absorbance, hopanes, and LG concentrations.

2.9.4 Harvard Impactor Maintenance

Subsequent to each sampling session, the Harvard Impactors were completely disassembled. All parts of the inside and outside were cleaned with Kimwipes and alcohol. The impaction plates were cleaned using soap distilled water and an ultrasonic cleaner for a minimum of 15 minutes. After sonication, the plates were rinsed thoroughly using distilled water (3 times) (Allen et al., 2014).

2.9.5 Optical Reflectance Analysis

All filters were analyzed at SPPH Occupational and Environmental Health Laboratory at the University of British Columbia for reflectance using a Diffusion Systems Ltd. Smoke Stain Reflectometer (M43D). After weighing the filters and prior to hopanes/LG analysis, the reflectance of all filters was measured. After cleaning the measuring head, mask, and standard plate with alcohol, the reflectometer was calibrated using five control filters. One filter was used to adjust the reflectometer to 100.0 followed by measuring. The other four control filters without adjusting the reflectometer reading. The control filter having the median reflectance value was selected as the primary control filter to be used to recalibrate the device after every 25 filters. After calibration, reflectance measurements were taken at five points across each filter (location previously decided). If the standard deviation (SD) of the collected data was over 0.5 units, the process was repeated again. A detailed protocol for measuring absorbance can be found in the supplemental SOP document (Allen et al., 2014).

2.9.6 Optical Reflectance and Absorbance

Reflectance values were converted to absorbance. The following formula was used to calculate absorbance before analysis:
\[ \alpha = \frac{A}{2V} \cdot \ln \left( \frac{R_f}{R_s} \right) \]

where \( \alpha \) is absorbance in \( 10^{-5} \) m\(^{-1} \), \( A \) is area of the filter in m\(^2\), \( V \) is volume sampled in m\(^3\), \( R_f \) is average reflectance of field blank filters, and \( R_s \) is reflectance of the sample filter as a percentage of 100.0.

### 2.9.7 HOPANES LABORATORY ANALYSIS

All filters were analyzed for Hopanes at SPPH Occupational and Environmental Health Laboratory at the University of British Columbia. Initially, each filter was cut in half using scissors, with each half placed in a separate clean Petri dish. Afterwards, the plastic ring was removed from one half of the filter and the filter was transferred to an extraction vessel (one for Hopane analysis and one for LG analysis). Approximately 1 mL of isooctane was added to the extraction vessel and ultrasonicated for 20 minutes. After spiking all samples with 50 \( \mu \)L of pyrene stock solution, each sample was transferred to gas chromatography (GC) vials for analysis. The analyses were conducted using gas chromatography mass spectrometry (GC-MS) as per study protocol XI in the supplementary SOP document (Allen et al., 2014). Finally, in order to reduce the number of missing values, hopane measurements <LOD were replaced with LOD/2 values for further analysis.

### 2.9.8 LG LABORATORY ANALYSIS

All filters were analyzed for LG at SPPH Occupational and Environmental Health Laboratory at the University of British Columbia. The previously prepared half of the filter was transferred to an extraction vessel. 2 mL of ethyl acetate was added to the vessel and it was then ultrasonicated for 30 minutes. 100 \( \mu \)L of the extract was transferred to GC vials; subsequently, pyridine (15 \( \mu \)L) and MSTFA in 1% TMCS solution (30 \( \mu \)L) was added to the vial. After vortexing the mixture for 10-20 seconds, the samples were placed in a dark location for at least 6 hours. As the last step before analyzing the samples, each vial was spiked by 10 \( \mu \)L of tri-isopropyl benzene. The analyses were conducted using GC-MS as per study protocol XII in the supplementary SOP document (Allen et al., 2014). Finally, in order to reduce the
number of missing values, LG measurements <LOD were replaced with LOD/2 values for further analysis.

2.9.9 Indoor Temperature and Relative Humidity (RH)

Indoor temperature and RH were logged continuously for both one-week periods using HOBO data loggers (UX100, Bourne, MA). One-minute averages of temperature and RH were collected. The test data were downloaded after each two-week period and measurements from the appropriate time were extracted for further analysis.

2.9.10 Time-Location-Activity Log

Participants were asked to complete a self-reported time-location-activity log at 30-minute intervals. The items in this log included participants’ locations (e.g. at home, commuting, etc.), mode of transport, proximity to potential sources of PM during the day (e.g. candles, cooking, tobacco, etc.), window and air conditioning status, and activities such as using a wood-burning stove.

This diary was used to identify other potential sources of exposure to PM that could affect the efficiency of HEPA filtration in addition to unusual peaks in results. It was expected that those who spend most of their time indoors at home would have the greatest impact from filtration especially since commuting can have a large impact on exposure to TRAP. Moreover, some medications and illnesses have been shown to affect systematic inflammation and endothelial function (Delfino et al., 2009; Pearson et al., 2003; Widlansky, Gokce, Keaney Jr, & Vita, 2003), hence participants were requested to complete a weekly health diary recording any medication and supplement intake in addition to any health symptoms.

2.10 Health Measurements

Various markers of inflammation were chosen based on previous research and the available literature. There are several cytokines involved in initiating an
inflammatory response including IL-6 (Gabay & Kushner, 1999; van Eeden, Yeung, Quinlam, & Hogg, 2005). This response involves other downstream inflammatory proteins such as CRP. Moreover, increased number of band cells in the blood suggests an increase in the activity of the bone marrow to initiate an inflammatory response (Swiston et al., 2008; Tan et al., 2000). Hence, CRP, IL-6, and BCC were included in this study to cover different components of the inflammatory response.

In addition to the main health measurements discussed below, general physiological measurements and variables were also collected. Self-reported age, height, and weight were recorded; BMI was calculated using the obtained information. For each study subject heart rate, systolic and diastolic blood pressures were measured at least 10 minutes before measuring endothelial function to avoid potential effects on microvascular endothelial function. Finally, indoor temperature at the time of conducting the EndoPAT was recorded since temperature might affect endothelial function measurements.

2.10.1 Microvascular Endothelial Function

As our primary endpoint, vascular function was evaluated at the end of the first week and at the end of the second week. In order to evaluate microvascular endothelial function, peripheral arterial tonometry (PAT) was performed using a portable EndoPAT 2000 device (Itamar Medical Ltd., Cesari, Israel). This device uses finger pneumatic sensors to detect changes in pulse wave amplitude (PWA) during a period of induced reactive hyperemia. EndoPAT 2000 was used as per the SOP provided by Itamar Medical Ltd. In short, the subjects were laid down in a dark and quiet room where pneumatic finger probes were attached to the index finger of each hand. Recordings were conducted by the device for 15 minutes, including a 5-minute baseline period, a 5-minute period with an inflated blood pressure cuff restricting blood flow, and a 5-min post-occlusion period. The reactive hyperemia index (RHI) score was then automatically calculated by built in algorithms in the EndoPAT 2000 software.
2.10.1.1 Post-Measurement Processing of EndoPAT Data

Generally, the algorithm embedded in the EndoPAT 2000 software automatically calculates an RHI score after each complete session. Data were screened to identify incomplete occlusion, noisy signal, and non-standard occlusion length and produce a “corrected” RHI score, if possible. Otherwise, the RHI score was used directly as calculated by the software.

For all participants and their EndoPAT evaluations, the PWA and software errors were manually inspected to find potential issues with the scores. For the results with non-standard occlusion length, the occlusion duration was manually set at 5:00 minutes by moving the end border in the software. In the case of having occlusion times >5:30 minutes, occlusion time was manually changed to 5:00 minutes (3 subjects only). The results were then re-analyzed by the software and an RHI score was produced.

2.10.2 Blood Collection, Processing, and Analysis

Blood samples were collected after EndoPAT measurements by a trained phlebotomist (1x10 ml gold SST and 1x6 ml lavender EDTA tube per participant). All blood samples were kept in a cooler with ice packs until transferred to the iCAPTURE laboratory at St. Paul’s Hospital for storage at -80° prior to analysis.

All blood samples were analyzed by the UBC James Hogg Research Centre at St. Paul’s Hospital. Blood samples were processed within 4-6 hours after collection. Blood sample processing involved obtaining a complete blood count report from the EDTA blood tube, preparation of Wright’s stain (EDTA tube), removal of SST serum (gold SST tube), removal of the EDTA plasma (EDTA tube), and the removal of the Buffy coat from EDTA tubes. Each of these fractions were then aliquoted into Eppendorf tubes and stored. The blood was analyzed for CRP, IL-6, and BCC, as markers of systematic inflammation. Blood sample collection, processing, and
analysis have been discussed in study protocols XIV and XV in the supplementary SOP document (Allen et al., 2014).

2.10.2.1 CRP

Samples were analyzed for CRP on a fluorescent-coded bead-based immunoassay testing platform, following the manufacturer’s protocol (R&D Systems, Catalog Number LUCB000) with the following modifications:

- Study plasma was used in the assay
- Samples were diluted 200-fold rather than the manufacturer's suggested 100-fold

Prior to plasma use in the assay, the samples were vortexed and centrifuged at 10,000x g for 1 minute in order to remove viscous material that might clog the filter plate and machine probe. Luminex 100 was used for all analysis.

2.10.2.2 IL-6

Similar to CRP analysis, the samples were analyzed on a fluorescent-coded bead-based immunoassay testing platform. The manufacturer’s protocol (Millipore HSCYTO-60SK) was used for IL-6 measurements with the following modification:

- Undiluted study plasma was used in the assay

Prior to plasma use in the assay, the samples were vortexed and centrifuged at 10,000x g for 1 minute in order to remove viscous material that might clog the filter plate and machine probe. Luminex 100 was used for all analysis.

2.10.2.3 BCC

Manual BCC was performed by a trained laboratory technician at the iCAPTURE laboratory at St. Paul’s Hospital, Vancouver, BC. Thin blood smears were prepared, dipped into methanol and air dried, and stained with Wright-Giemsa stain (Bayer
HEMA-TEK 2000 Slide Stainer, Leverkusen, Germany) and counted under the 40x objective of a light microscope.

**2.11 Statistical Analysis**

For the purposes of this study, Excel 2011 was used to prepare the initial and final database. JMP® 10 (SAS Institute Inc., Cary, NC) was used to conduct all required statistical analyses.

**2.11.1 Data Cleaning and Descriptive Statistics**

Prior to data analysis, all datasets were reviewed to ensure quality. In general, individuals with incomplete or poor quality data for one or both of the sessions were excluded from final analysis. This approach enabled a “cleaner” data analysis with matched data and without having to account for characteristics such as age, BMI, and sex.

**2.11.1.1 Exposure Data**

First, any homes with incomplete exposure data collections were marked as “excluded”. PM$_{2.5}$ sampling data were then reviewed to ensure appropriate sampling times and flow rates for the duration of the study. Technician’s sampling logs were inspected to detect any irregularities in sampling which warranted the exclusion of data points from the analysis. Samples were excluded if any of the following applied:

- The tube was disconnected from the pump at any point during the study,
- The sampling pump had failed,
- The sampling period was less than 9,000 minutes per week of sampling (90% of a week),
- The pump flow rate was found to be 10% higher or lower than the initial 10L/min, (e.g. disconnected hose, pump failure, and short sampling period)
2.11.1.2 Health Data

As with the exposure data, any health variable with incomplete information for either or both sessions was marked as “excluded” for that particular health endpoint analysis. Moreover, the EndoPAT records were reviewed to ensure proper occlusion time and the absence of background PWA noise.

2.11.2 Distribution of Exposure and Health Variables

Box plots of all exposure and health variables were produced using JMP® 10 to examine the normality of the distribution and also the presence of outliers. For log-normally distributed health variables (i.e. outcome variables), the data were log-transformed before any subsequent analysis. Moreover, descriptive statistics were tabulated for exposure and health variables.

2.11.3 Extreme Values

For outliers lying outside mean ± 2SD of all relevant variable values in the dataset, the spreadsheets were reviewed and compared to field notes to ensure the accuracy of each data point. Weekly diaries were also checked for other potential sources that could have affected values (e.g. indoor smoking, wood burning, infections, etc.). If feasible, gravimetric and laboratory analyses were re-done to ensure that the results of both analyses match. Finally, if no reasonable and logical explanation for extreme values was available, they were included in the analysis but were marked for potential sensitivity analysis.

2.11.4 Scaling Exposure Contrasts

In order to compare the magnitude of the effects across different exposure (i.e. PM$_{2.5}$, hopanes, LG, and absorbance), the exposure contrasts were scaled to the median within-home change between filter and no filter conditions. In order to achieve this, change in exposure from filter to no filter was calculated for all homes with complete exposure and health data. Subsequently, all respective measurements were divided by the median value of change in exposure among all homes.
2.11.5 Evaluation of Difference Between Home Types and Filtration Status

To further characterize the significance of differences in various exposure and health variables between TRAP and WS homes and filtration/no filtration sessions, paired t-tests were performed. To illustrate the general characteristics and homogeneity of the participants in each home type, summary statistics of study population characteristics (e.g. age, BMI, blood pressure, % time at home, etc.) were calculated. Moreover, summary of exposure characteristics (e.g. PM$_{2.5}$, absorbance, LG, hopanes, etc.) were calculated by HEPA filtration status and home type. The same procedure was followed for the health outcomes included in this study (e.g. RHI, CRP, IL-6, BCC, and %PMN).

2.11.6 Mixed Model Analysis

Mixed models were used to properly account for measurements clustered within participants and participants clustered within homes. Due to the crossover design of this study and the fact that only individuals with complete data for both sessions (i.e. paired data) were included in the final analysis, there was no need to include time invariate variables (e.g. age, sex and BMI) in the model to account for potential confounding. Thus, we included only time-varying adjustment variables (Subject ID, Home ID, and average indoor temperature) in the model. The general mixed model for measurement $i$ on participant $j$ living in home $k$ was:

$$\log Y_{ijk} = \alpha_j + \gamma_k + \beta_0 + \beta_1 \text{HEPA}_{ijk} + \beta_2 \text{Ind.Temp}_{ijk} + e_{ijk}$$

where $\alpha_j$ and $\gamma_k$ are random participant- and home-specific intercepts, respectively, and $\beta_1$ represents the fixed effect of HEPA filtration on the log-transformed outcome variable, $\log Y_{ijk}$. The HEPA variable was replaced with other continuous exposure variables (e.g. PM$_{2.5}$ concentration, LG concentration, etc.) for different models. $\beta_2$ represents the fixed effect of average indoor temperature on the log-transformed outcome variable, $\log Y_{ijk}$.  


Mixed models were prepared for the \textit{a priori} primary outcome variable of this study, which was RHI. Several other mixed models were created using secondary outcome variables including CRP, IL-6, BCC, and \%PMN. RHI, CRP, and IL-6 were log-transformed since they were skewed. For each of these outcome variables, four exposure variables were included in the models: HEPA filtration status (binary), and absorbance, LG, and PM$_{2.5}$ (continuous).

In order to evaluate the differences in health effects of exposures between TRAP and WS homes, the following model was used:

$$\log Y_{ijk} = \alpha_j + \gamma_k + \beta_0 + \beta_1 \text{HEPA}_{ijk} + \beta_2 \text{Group}_{ijk} + \beta_3 (\text{HEPA} \times \text{Group})_{ijk} + \beta_4 \text{Ind.Temp}_{ijk} + e_{ijk}$$

where “Group” is a binary variable representing WS or traffic exposed homes.

Table 2-2 below summarizes the main mixed effect models that were used in this study. For each of the listed explanatory variables, a separate mixed model was prepared.

40
### Table 2-2 Summary of the mixed effect models used in the analysis

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Explanatory Variables</th>
<th>Control for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log RHI</td>
<td>• HEPA</td>
<td>• Subject and Home ID (Random effect)</td>
</tr>
<tr>
<td></td>
<td>• PM$_{2.5}$</td>
<td>• Avg. indoor temperature (Fixed effect)</td>
</tr>
<tr>
<td></td>
<td>• Absorbance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• LG</td>
<td></td>
</tr>
<tr>
<td>Log CRP</td>
<td>• HEPA</td>
<td>• Subject and Home ID (Random effect)</td>
</tr>
<tr>
<td></td>
<td>• PM$_{2.5}$</td>
<td>• Avg. indoor temperature (Fixed effect)</td>
</tr>
<tr>
<td></td>
<td>• Absorbance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• LG</td>
<td></td>
</tr>
<tr>
<td>Log IL-6</td>
<td>• HEPA</td>
<td>• Subject and Home ID (Random effect)</td>
</tr>
<tr>
<td></td>
<td>• PM$_{2.5}$</td>
<td>• Avg. indoor temperature (Fixed effect)</td>
</tr>
<tr>
<td></td>
<td>• Absorbance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• LG</td>
<td></td>
</tr>
<tr>
<td>BCC</td>
<td>• HEPA</td>
<td>• Subject and Home ID (Random effect)</td>
</tr>
<tr>
<td></td>
<td>• PM$_{2.5}$</td>
<td>• Avg. indoor temperature (Fixed effect)</td>
</tr>
<tr>
<td></td>
<td>• Absorbance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• LG</td>
<td></td>
</tr>
<tr>
<td>%PMN</td>
<td>• HEPA</td>
<td>• Subject and Home ID (Random effect)</td>
</tr>
<tr>
<td></td>
<td>• PM$_{2.5}$</td>
<td>• Avg. indoor temperature (Fixed effect)</td>
</tr>
<tr>
<td></td>
<td>• Absorbance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• LG</td>
<td></td>
</tr>
</tbody>
</table>

### 2.11.7 Effect Modification by Age, BMI, and Gender

The possibility of effect modification by age, BMI, and sex was also explored in stratified analyses. Each of these variables were converted to binary variables using median age (above and below 42 years old), normal BMI (above and below 25 kg/m$^2$), and sex.

### 2.11.8 Interpreting Effect Estimates from Log Transformed Models

Interpreting the results of a regression model when the outcome variable is log-transformed is not as simple as looking at the effect estimates. Interpretation of such models can be challenging since back transforming the estimates will not be sufficient either. In order to interpret the log-transformed outcomes the following formula was used:

\[
\text{% change in outcome per 1-unit change in predictor} = 100 \times (e^\beta - 1)
\]
where $\beta$ is the effect estimate for the exposure of interest (e.g. PM$_{2.5}$). Using this formula and by scaling exposure contrasts as discussed above, we can report the results of the model as % change in outcome per unit median change in exposure.
3 Results

Overall, 13,200 invitation letters were mailed out to residences in the targeted postal codes across Greater Vancouver Region. From those who called back requesting information from the study coordinator and responding to screening interview questions, 83 subjects between the ages of 19-72 years old (54 from TRAP homes and 29 from WS homes) living in 44 different residences, met the inclusion criteria for this study. Twenty-eight homes were located in high-TRAP areas and sixteen were in high-WS areas.

3.1 Summary Statistics – Participants with Complete Data

Overall, out of 83 participants, 68 individuals with complete data for all exposure and health outcome variables of interest were included in the RHI analysis; forty-eight of these subjects lived in high TRAP homes while 20 lived in high WS homes (Figure 3-1). Of the 15 excluded participants, 11 were excluded due to sampling duration not meeting the criteria of this study (i.e. 90% of the week), 2 due to filter damage, 1 due to participant drop out, and 1 due to missing pump data (exposure calculation not possible). There were also 2 individuals with missing RHI measures, which overlapped with exposure exclusions. For CRP, IL-6, and BCC models, 15 participants were excluded due to exposure data issues (mentioned above) and an additional 16 participants due to the lack of blood work data for either or both sampling sessions. Of the 16 individuals with missing CRP, IL-6, and BCC, 4 participants were excluded due to inability to process the samples (laboratory closure), 10 participants excluded for the lack of blood samples (no samples collected), and 2 participants excluded since insufficient blood was collected. All participants had a mean (±SD) age of 43.8 ± 12.8 years and 53% were female. There were also approximately equal numbers of male and female participants in both TRAP and WS homes. The WS exposure participants were significantly older (mean age 40.8 years vs. 51.3 years) and spent slightly more time indoors at home but the two groups did not differ in any other measured characteristics (Table 3-1). The age range for all participants was between 19 to 72 years old.
Table 3-1 summarizes study population characteristics for all participants and also participants stratified by home type. P-values reflect t-test for TRAP versus WS.

**Table 3-1 Summary of study population characteristics with complete data**

<table>
<thead>
<tr>
<th>Study Population Characteristics</th>
<th>All Participants (Mean ± SD) N=68</th>
<th>TRAP Exposed Participants (Mean ± SD) n=48</th>
<th>WS Exposed Participants (Mean ± SD) n=20</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>43.8 ± 12.8</td>
<td>40.8 ± 12.3</td>
<td>51.3 ± 10.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>% Female</td>
<td>53%</td>
<td>54%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>24.9 ± 4.0</td>
<td>24.9 ± 3.9</td>
<td>25.0 ± 4.3</td>
<td>0.73</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>119.8 ± 13.3</td>
<td>119.9 ± 14.1</td>
<td>119.4 ± 11.7</td>
<td>0.81</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>75.6 ± 10.5</td>
<td>75.4 ± 10.9</td>
<td>76.1 ± 9.5</td>
<td>0.83</td>
</tr>
<tr>
<td>% Time at Home</td>
<td>74.4 ± 13.3</td>
<td>73.6 ± 12.8</td>
<td>76.3 ± 14.3</td>
<td>0.076</td>
</tr>
<tr>
<td>Baseline CRP (mg/L)</td>
<td>2.6 ± 3.6</td>
<td>2.3 ± 2.6</td>
<td>3.05 ± 5.07</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Mean BMI was approximately 25 for each group, which reflects the high end of normal BMI. Mean systolic and diastolic blood pressures were equal and within the range of normal blood pressure at <120 mmHg and <80 mmHg, respectively. On average, all participants spent about three-fourth of their time at home with both groups being similar; this is particularly important since the greater amount of time participants spent at home, the greater the potential effect of HEPA filtration on their health. Furthermore, it should be noted that the baseline CRP levels were not significantly different between the two groups.
3.2 Summary Statistics – Participants with Incomplete Data

After reviewing all the required data for running mixed statistical models, 15 participants had incomplete data for RHI models, missing values for one or more of the variables needed. It is important to note that with regards to outcome variables, if a subject was missing a value, that person was excluded only for the model including that specific outcome variable. For example, if subject 1 was missing an RHI measurement, he was only excluded from the RHI model and not models including CRP or IL-6. The same analogy was used for deciding to exclude participants for the lack of exposure variables. In order to compare the population characteristics of those with incomplete data with those with complete data, summary statistics were prepared for those with incomplete data. Table 3-2, provides a summary of the differences in population characteristics between participants with complete and incomplete data. As seen in this table, the study population with incomplete data is similar to those with complete data, with no statistically significant differences between the two groups. It is worth mentioning that BMI and % time at home are borderline significantly different between the two groups. Overall, we can assume that we have not selectively excluded individuals with different characteristics and potentially affecting the outcomes.
Table 3-2 Comparison of study population characteristics between participants with complete and incomplete data for RHI

<table>
<thead>
<tr>
<th>Complete vs. Incomplete Data Study Population Characteristics</th>
<th>Complete Data (Mean ± SD) N=68</th>
<th>Incomplete Data (Mean ± SD) N=15</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>43.8 ± 12.8</td>
<td>42.1 ± 8.47</td>
<td>0.47</td>
</tr>
<tr>
<td>% Female</td>
<td>53%</td>
<td>50%</td>
<td>---</td>
</tr>
<tr>
<td>BMI</td>
<td>24.9 ± 4.0</td>
<td>23.4 ± 3.4</td>
<td>0.06</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>119.8 ± 13.3</td>
<td>117.0 ± 14.9</td>
<td>0.46</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>75.6 ± 10.5</td>
<td>76.0 ± 10.1</td>
<td>0.81</td>
</tr>
<tr>
<td>% Time at Home</td>
<td>74.4 ± 13.3</td>
<td>69.4 ± 18.1</td>
<td>0.07</td>
</tr>
<tr>
<td>Baseline CRP (mg/L)</td>
<td>2.6 ± 3.6</td>
<td>2.03 ± 2.63</td>
<td>0.27</td>
</tr>
</tbody>
</table>

3.3 Exposure Characteristics

Table 3-3 provides a summary of different exposure characteristics stratified by HEPA filtration status. General outdoor PM$_{2.5}$ levels were similar in two sampling sessions confirming the absence of variability between sampling periods. With the implementation of indoor HEPA filters, 85% of the homes had reductions in PM$_{2.5}$ concentrations and 15% of the homes having increase in PM$_{2.5}$ levels; all WS homes had reduced levels while 79% of TRAP homes had dropped PM$_{2.5}$ levels. There was a statistically significant reduction of over 40% in PM$_{2.5}$ concentrations with a drop of 36% in TRAP homes and 48% in WS homes. Similar to PM$_{2.5}$, an approximately 8% reduction in absorbance was found which was also statistically significant. No such relationship was found with regards to hopanes and LG as the markers of TRAP and WS, respectively. However, considering the median values for indoor hopanes and LG, there was a clear decreasing trend in concentrations with HEPA filtration.

Variations in outdoor temperatures can potentially affect air pollution concentrations indoors as a result of increased infiltration into residences (Allen et
al., 2012). However, the results of the current study indicate that outdoor temperatures were quite stable and similar between the filtration and no filtration weeks reducing the potential for variations in infiltration between the two sessions. Moreover, % time spent at home or in transit was statistically similar during filtration and no filtration weeks indicating similar filtration exposure and similar exposure to other sources of PM$_{2.5}$ outside home.
Table 3-3 Summary of exposure characteristics by HEPA filtration status

<table>
<thead>
<tr>
<th>Exposure Characteristics</th>
<th>HEPA Off</th>
<th>HEPA On</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Median</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Outdoor Temp. (°C)</td>
<td>10.7 ± 5.2</td>
<td>10.8</td>
<td>10.5 ± 5.4</td>
</tr>
<tr>
<td>Indoor Temp. (°C)</td>
<td>20.9 ± 2.2</td>
<td>21.0</td>
<td>20.9 ± 2.3</td>
</tr>
<tr>
<td>PM$_{2.5}$ Outdoors (µg/m$^3$)</td>
<td>5.7 ± 2.8</td>
<td>5.5</td>
<td>5.4 ± 2.2</td>
</tr>
<tr>
<td>PM$_{2.5}$ Indoors (µg/m$^3$)</td>
<td>7.1 ± 6.1</td>
<td>7.5</td>
<td>4.3 ± 2.6</td>
</tr>
<tr>
<td>LG Outdoors (ng/m$^3$)</td>
<td>17.9 ± 47.8</td>
<td>3.5</td>
<td>11.2 ± 17.12</td>
</tr>
<tr>
<td>LG Indoors (ng/m$^3$)</td>
<td>13.8 ± 36.5</td>
<td>2.5</td>
<td>10.1 ± 16.3</td>
</tr>
<tr>
<td>Indoor Absorbance</td>
<td>2.25 ± 0.25</td>
<td>2.20</td>
<td>2.08 ± 0.21</td>
</tr>
<tr>
<td>Outdoor Absorbance</td>
<td>3.08 ± 2.70</td>
<td>2.25</td>
<td>2.30 ± 1.26</td>
</tr>
<tr>
<td>Hopanes Indoors (pg/m$^3$)</td>
<td>226.8 ± 245.6</td>
<td>132.5</td>
<td>207.8 ± 227.8</td>
</tr>
<tr>
<td>Hopanes Outdoors (pg/m$^3$)</td>
<td>198.9 ± 209.6</td>
<td>93.4</td>
<td>146.4 ± 157.9</td>
</tr>
<tr>
<td>% Time at Home</td>
<td>74.3 ± 13.7</td>
<td>75.0</td>
<td>75.6 ± 12.8</td>
</tr>
<tr>
<td>% Time in Transit</td>
<td>2.95 ± 3.51</td>
<td>2.38</td>
<td>2.86 ± 2.56</td>
</tr>
</tbody>
</table>
The SDs of indoor and outdoor concentrations of hopanes and LG were quite wide. This observation was due to the presence of large outliers in each of these variables for which there was no reasonable explanation to exclude from the analysis. As with any other laboratory analysis procedure, hopane and LG concentration measurement was limited by a method limit of detection (LOD). Overall, the concentration of hopanes was less than the LOD for 38.2% of the filters. For LG, 16.5% of the filters had concentrations less than the method LOD.

This might have lead to biased values undermining the usefulness of such data. Moreover, there was clear relationship between temperature and hopane concentrations, which further complicated interpretation of the hopane measurements. Hence, we decided to use hopane data exclusively for confirming the categorization of postal codes into TRAP or WS for participant recruitment.

To better characterize different exposures, exposures were stratified by home type and HEPA filtration. Table 3-4 summarizes exposure characteristics in TRAP- and WS-exposed homes. Mean indoor and outdoor PM2.5 levels were not significantly different between TRAP and WS homes. Indoor absorbance was significantly higher in high-TRAP homes (p-value <0.05) compared to those in the high-WS areas. Although not statistically significant, both indoor and outdoor LG levels were greater in WS homes. Median outdoor LG levels were approximately three times greater in WS areas compared to TRAP areas. Hopanes measurements also have large SD with non-significant differences between TRAP and WS homes. However, both indoor and outdoor median hopane levels in TRAP homes were over twice that of WS homes.

Both mean indoor and outdoor temperatures are different between the two groups (P-value = 0.0001). Mean outdoor temperature was lower in WS homes due to the fact that wood is primarily used during the colder months of the year for heating, which is when sampling was conducted. The same reasoning can be applied to the small drop in mean indoor temperature for WS homes.
Based on the results from paired t-tests, mean % time spent at home and mean % time spent in transit are equal between TRAP and WS homes with p-values greater than 0.05. It is also worth mentioning that participants in both TRAP and WS homes spent approximately 75% of their time at home; this implies similar exposure to HEPA filtration at home.
Table 3-4 Summary of exposure characteristics by home type (No HEPA)

<table>
<thead>
<tr>
<th>Exposure Characteristics</th>
<th>TRAP</th>
<th>WS</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Median</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Outdoor Temp. (°C)</td>
<td>12.8 ± 4.5</td>
<td>13.2</td>
<td>5.6 ± 2.5</td>
</tr>
<tr>
<td>Indoor Temp. (°C)</td>
<td>21.7 ± 2.1</td>
<td>22.0</td>
<td>19.1 ± 1.11</td>
</tr>
<tr>
<td>PM$_{2.5}$ Outdoors (µg/m$^3$)</td>
<td>6.01 ± 2.91</td>
<td>5.62</td>
<td>5.03 ± 2.51</td>
</tr>
<tr>
<td>PM$_{2.5}$ Indoors (µg/m$^3$)</td>
<td>7.31 ± 2.06</td>
<td>7.64</td>
<td>6.54 ± 2.66</td>
</tr>
<tr>
<td>LG Outdoors (ng/m$^3$)</td>
<td>19.5 ± 54.3</td>
<td>2.86</td>
<td>13.2 ± 13.5</td>
</tr>
<tr>
<td>LG Indoors (ng/m$^3$)</td>
<td>8.46 ± 14.7</td>
<td>2.51</td>
<td>29.3 ± 67.1</td>
</tr>
<tr>
<td>Indoor Absorbance</td>
<td>2.21 ± 0.19</td>
<td>2.20</td>
<td>2.05 ± 0.29</td>
</tr>
<tr>
<td>Hopanes Indoors (pg/m$^3$)</td>
<td>239.8 ± 274.9</td>
<td>132.5</td>
<td>198.8 ± 168.8</td>
</tr>
<tr>
<td>Hopanes Outdoors (pg/m$^3$)</td>
<td>228.3 ± 221.6</td>
<td>142.1</td>
<td>267.3 ± 451.3</td>
</tr>
<tr>
<td>% Time at Home</td>
<td>73.3 ± 13.1</td>
<td>74.6</td>
<td>76.6 ± 15.2</td>
</tr>
<tr>
<td>% Time in Transit</td>
<td>2.91 ± 2.86</td>
<td>2.38</td>
<td>3.05 ± 4.75</td>
</tr>
</tbody>
</table>
Finally, Table 3-5 provides a summary of the effect of HEPA filtration on various exposures in both TRAP- and WS-exposed homes. Indoor PM$_{2.5}$ concentrations were reduced in both TRAP and WS homes to different extents with an approximately 36% drop in PM$_{2.5}$ in TRAP homes and 48% in WS homes. Mean outdoor PM$_{2.5}$ levels were very close in TRAP and WS homes for both HEPA versus no HEPA weeks. With wide confidence intervals, there are no clear trends for HEPA filtration effectiveness with regards to hopanes and LG in either home type. There appears to be a small decrease in indoor absorbance in TRAP homes.
# Table 3-5 Summary of exposure characteristics by HEPA filtration status and home type

<table>
<thead>
<tr>
<th>HEPA Status</th>
<th>TRAP</th>
<th></th>
<th>WS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Median</td>
<td>Mean ± SD</td>
<td>Median</td>
</tr>
<tr>
<td><strong>Indoor PM$_{2.5}$</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off</td>
<td>7.32 ± 2.05</td>
<td>7.64</td>
<td>6.54 ± 2.66</td>
<td>6.68</td>
</tr>
<tr>
<td>On</td>
<td>4.69 ± 2.76</td>
<td>4.29</td>
<td>3.37 ± 1.93</td>
<td>2.51</td>
</tr>
<tr>
<td><strong>Outdoor PM$_{2.5}$</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off</td>
<td>6.01 ± 2.90</td>
<td>5.62</td>
<td>5.03 ± 2.51</td>
<td>4.81</td>
</tr>
<tr>
<td>On</td>
<td>6.05 ± 1.97</td>
<td>5.89</td>
<td>3.88 ± 2.06</td>
<td>4.01</td>
</tr>
<tr>
<td><strong>Indoor Hopanes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off</td>
<td>239.88 ± 274.9</td>
<td>132.48</td>
<td>198.7 ± 168.8</td>
<td>109.3</td>
</tr>
<tr>
<td>On</td>
<td>229.8 ± 251.2</td>
<td>215.91</td>
<td>160.70 ± 162.44</td>
<td>54.9</td>
</tr>
<tr>
<td><strong>Outdoor Hopanes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off</td>
<td>228.3 ± 274.9</td>
<td>142.1</td>
<td>2873.5 ± 87612.1</td>
<td>54.77</td>
</tr>
<tr>
<td>On</td>
<td>119.5 ± 89.2</td>
<td>113.2</td>
<td>201.47 ± 239.45</td>
<td>55.01</td>
</tr>
<tr>
<td><strong>Indoor LG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off</td>
<td>8.46 ± 14.71</td>
<td>2.51</td>
<td>29.3 ± 67.05</td>
<td>3.94</td>
</tr>
<tr>
<td>On</td>
<td>9.39 ± 17.13</td>
<td>1.38</td>
<td>11.8 ± 14.37</td>
<td>5.00</td>
</tr>
<tr>
<td><strong>Outdoor LG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off</td>
<td>19.5 ± 54.3</td>
<td>2.86</td>
<td>13.18 ± 13.5</td>
<td>4.58</td>
</tr>
<tr>
<td>On</td>
<td>8.37 ± 15.31</td>
<td>3.32</td>
<td>20.6 ± 19.9</td>
<td>15.12</td>
</tr>
<tr>
<td><strong>Indoor Absorbance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off</td>
<td>2.29 ± 0.14</td>
<td>2.32</td>
<td>2.15 ± 0.38</td>
<td>1.98</td>
</tr>
<tr>
<td>On</td>
<td>2.14 ± 0.21</td>
<td>2.11</td>
<td>1.94 ± 0.10</td>
<td>1.96</td>
</tr>
<tr>
<td><strong>Outdoor Absorbance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Off</td>
<td>3.15 ± 2.86</td>
<td>2.34</td>
<td>2.90 ± 2.28</td>
<td>2.11</td>
</tr>
<tr>
<td>On</td>
<td>2.37 ± 0.23</td>
<td>2.34</td>
<td>2.15 ± 0.27</td>
<td>2.11</td>
</tr>
</tbody>
</table>

As expected, there was higher indoor absorbance in TRAP homes compared to WS homes, with small reductions in both home types with HEPA filtration. With regards
to absorbance, there seems to be a variation between HEPA and no HEPA weeks but it should be noted that during the week with no filtration, there is a fairly large confidence interval for both home types compared to the week with filtration.

As predicted, WS homes were over 7 times further away from highway or major road compared to TRAP homes. Moreover, TRAP homes had on average 8 times more road length in their 100-meter buffer (Table 3-6). Overall, higher concentrations of indoor and outdoor LG were present in WS homes, though not statistically significant. All together, we were able to verify that homes were categorized into their respective categories correctly.

Table 3-6 Summary statistics to confirm categorization of TRAP and WS homes

<table>
<thead>
<tr>
<th>Traffic and Woodsmoke Home Categorization</th>
<th>All Homes</th>
<th>TRAP Homes</th>
<th>WS Homes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Median</td>
<td>Mean ± SD</td>
<td>Median</td>
</tr>
<tr>
<td>Indoor Levoglucosan (ng/m³)</td>
<td>11.9 ± 28.7</td>
<td>2.42</td>
<td>8.9 ± 15.8</td>
</tr>
<tr>
<td>Outdoor Levoglucosan (ng/m³)</td>
<td>14.5 ± 35.7</td>
<td>3.62</td>
<td>13.8 ± 39.7</td>
</tr>
<tr>
<td>Distance to Nearest HW or MR (meters)</td>
<td>129.9 ± 181.3</td>
<td>45.3</td>
<td>50.5 ± 47.3</td>
</tr>
<tr>
<td>HW or MR length in 100m Buffer (meters)</td>
<td>162.8 ± 136.1</td>
<td>181.1</td>
<td>209.9 ± 120.9</td>
</tr>
</tbody>
</table>

3.4 Health Outcomes

As with exposure characteristics, summary statistics were also prepared for different health outcomes included in this study (Tables 3-7 and 3-8). Table 3-7 summarizes mean (±SD) and median of health outcomes stratified by HEPA filtration status. Based on the basic statistics and p-values presented in Table 3-7
below, there was no statistically significant difference between any of the health outcomes with HEPA filtration.

Table 3-7 Summary of health outcomes by HEPA filtration status

<table>
<thead>
<tr>
<th>Health Outcomes</th>
<th>HEPA Off</th>
<th>HEPA On</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ±</td>
<td>Median</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>RHI</td>
<td>2.14 ± 0.62</td>
<td>2.11</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>2.37 ± 3.34</td>
<td>1.21</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>2.99 ± 5.24</td>
<td>1.46</td>
</tr>
<tr>
<td>BCC</td>
<td>0.82 ± 0.81</td>
<td>1</td>
</tr>
<tr>
<td>% PMN</td>
<td>2.78 ± 0.92</td>
<td>2.69</td>
</tr>
</tbody>
</table>

3.5 Mixed Model Results

After reviewing all collected data, 68 participants were included in mixed models including RHI as their outcome variable, forty-eight of whom lived in high-TRAP homes and twenty lived in high-WS homes. With regards to CRP models, 52 participants had complete data required for inclusion in the models. It should be noted that all effect estimates of log-transformed models (i.e. RHI, CRP, and IL-6) were converted to % change to facilitate interpretation of results. Moreover, average indoor temperature (fixed effect), and home and subject ID (random effects) were included in all models.
3.6 HEPA Filtration

Table 3-9 summarizes the model estimates of change in health outcomes with HEPA filtration. Results are presented for all homes, TRAP homes only, and WS homes only.

<table>
<thead>
<tr>
<th></th>
<th>RHI</th>
<th>CRP</th>
<th>IL-6</th>
<th>BCC</th>
<th>%PMN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% Change (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Change (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>All Homes</strong></td>
<td>-0.68 (-2.5, 2.6)</td>
<td>-0.67 (-26.7, 34.6)</td>
<td>3.97 (-25.9, 47.9)</td>
<td>0.03 (-0.25, 0.33)</td>
<td>0.03 (-0.25, 0.32)</td>
</tr>
<tr>
<td><strong>TRAP Homes Only</strong></td>
<td>-2.5 (-11.3, 6.98)</td>
<td>2.75 (-28.7, 48.5)</td>
<td>8.03 (-27.6, 61.3)</td>
<td>-0.07 (-0.45, 0.31)</td>
<td>0.13 (-0.24, 0.51)</td>
</tr>
<tr>
<td><strong>WS Homes Only</strong></td>
<td>2.6 (-9.23, 15.9)</td>
<td>-4.46 (-43.5, 19.4)</td>
<td>-8.62 (-45.8, 54.2)</td>
<td>0.22 (-0.25, 0.69)</td>
<td>-0.16 (-0.63, 0.32)</td>
</tr>
</tbody>
</table>

The initial hypothesis was that with the implementation of HEPA filtration, there would be an improvement in endothelial function and systematic inflammation (i.e. an increase in RHI score and reductions in markers of inflammation). For RHI, there was no association with HEPA filtration. There was also no association between CRP and IL-6 and HEPA filtration in either of the groups. Neither BCC nor %PMN showed statistically significant associations with HEPA filtration. The effect estimates were extremely small with very large confidence intervals. Overall, there were no significant associations between HEPA filtration and RHI, CRP, IL-6, BCC, or %PMN.

3.7 PM$_{2.5}$

Table 3-10 summarizes the model estimates of change in health outcomes per unit median increase in PM$_{2.5}$ concentration. As described in the Methods section, all exposure contrasts were scaled to the within-home change between HEPA and no HEPA conditions. Hence, all changes in health outcomes are considered to be change per unit median increase in exposure. Results are presented for all homes, TRAP homes only, and WS homes only.
Table 3-9 Change in health outcomes per unit median change in PM$_{2.5}$

<table>
<thead>
<tr>
<th></th>
<th>RHI</th>
<th>CRP</th>
<th>IL-6</th>
<th>BCC</th>
<th>%PMN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Change (95% CI)</td>
<td>Change (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>All Homes</strong></td>
<td>2.8 (-1.3, 7.2)</td>
<td>7.8 (-7.9, 26.2)</td>
<td>-3.1 (-14.4, -2.7)</td>
<td>-0.03 (-0.19, 0.12)</td>
<td>0.11 (-0.03, 0.21)</td>
</tr>
<tr>
<td><strong>TRAP Homes Only</strong></td>
<td>3.5 (-1.4, 8.1)</td>
<td>18.4 (-0.24, 40.6)</td>
<td>-2.7 (-15.5, 11.9)</td>
<td>-0.02 (-0.21, 0.17)</td>
<td>0.11 (-0.07, 0.29)</td>
</tr>
<tr>
<td><strong>WS Homes Only</strong></td>
<td>0.97 (-7.6, 10.4)</td>
<td>-16.8 (-42.1, 19.4)</td>
<td>-14.4 (-41.6, 25.5)</td>
<td>-0.05 (-0.33, 0.24)</td>
<td>0.07 (-0.16, 0.31)</td>
</tr>
</tbody>
</table>

With regards to PM$_{2.5}$ exposure, we expected the deterioration of microvascular endothelial function and systematic inflammation (i.e. a decrease in RHI score and increases in markers of inflammation). With regards to RHI, there was no association found with PM$_{2.5}$ concentrations. However, a non-significant increase in CRP was observed per unit median increase in PM$_{2.5}$ for all homes. After stratifying by home type, there was an 18.4% increase in CRP levels per unit median increase in PM$_{2.5}$, which had a borderline statistical significance. No such effect was found in WS homes with the effect estimate in the opposite direction of TRAP homes.

For IL-6, there were no significant associations with PM$_{2.5}$ concentrations in either TRAP or WS homes. Finally, there was no significant increase in BCC or %PMN with increases in PM$_{2.5}$ levels. Overall, there was some suggestion of an association between PM$_{2.5}$ exposure and CRP levels among individuals residing in TRAP homes.

### 3.8 Absorbance

Table 3-11 summarizes the model estimates of change in health outcomes per unit median increase in absorbance. Results are presented for all homes, TRAP homes only, and WS homes only.
Table 3-10 Change in health outcomes per unit median change in absorbance

<table>
<thead>
<tr>
<th></th>
<th>RHI</th>
<th>CRP</th>
<th>IL-6</th>
<th>BCC</th>
<th>%PMN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Change (95% CI)</td>
<td>Change (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>All Homes</strong></td>
<td>2.03 (-0.85, 5.01)</td>
<td>-1.24 (-15.7, 15.7)</td>
<td>0.45 (-12.4, 15.1)</td>
<td>-0.026 (-0.13, 0.08)</td>
<td>0.08 (-0.05, 0.21)</td>
</tr>
<tr>
<td><strong>TRAP Homes Only</strong></td>
<td>4.15 (-0.003, 8.48)</td>
<td>5.02 (-11.5, 24.6)</td>
<td>-2.2 (-14.4, 11.7)</td>
<td>0.018 (-0.14, 0.18)</td>
<td>0.06 (-0.11, 0.23)</td>
</tr>
<tr>
<td><strong>WS Homes Only</strong></td>
<td>0.19 (-4.74, 5.38)</td>
<td>0.19 (-40.5, 25.9)</td>
<td>-11.7 (-40.2, 30.4)</td>
<td>-0.10 (-0.26, 0.06)</td>
<td>0.03 (-0.17, 0.24)</td>
</tr>
</tbody>
</table>

A non-significant improvement in RHI was found with absorbance in both TRAP and WS homes. TRAP homes demonstrated a borderline statistical significance. However, there was no significant association between CRP levels and absorbance in any of the subgroups. With regards to IL-6, there was no significant relationship with absorbance. Finally, there was no significant association between BCC/%PMN and absorbance, with very small non-significant effect estimates for both health endpoints. Overall, there were no significant associations between absorbance and RHI, CRP, IL-6, BCC, or %PMN. However, there were some suggestions of an association between RHI and TRAP absorbance.

3.9 LG

Table 3-12 summarizes the model estimates of change in health outcomes per unit median increase in LG. Results are presented for all homes, TRAP homes only, and WS homes only.
Table 3-11 Change in health outcomes per unit median change in LG

<table>
<thead>
<tr>
<th></th>
<th>RHI % Change (95% CI)</th>
<th>CRP % Change (95% CI)</th>
<th>IL-6 % Change (95% CI)</th>
<th>BCC Change (95% CI)</th>
<th>%PMN Change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Homes</td>
<td>-0.0095 [-0.05, 0.03]</td>
<td>-0.13 [-0.35, 0.078]</td>
<td>-0.06 [-0.26, 0.14]</td>
<td>-0.00018 [-0.002, 0.001]</td>
<td>0.0009 [-0.001, 0.003]</td>
</tr>
<tr>
<td>TRAP Homes Only</td>
<td>-0.043 [-0.14, 0.058]</td>
<td>-0.19 [-0.52, 0.24]</td>
<td>0.13 [-0.21, 0.48]</td>
<td>-0.0024 [-0.006, 0.001]</td>
<td>0.0023 [-0.001, 0.006]</td>
</tr>
<tr>
<td>WS Homes Only</td>
<td>0.003 [-0.059, 0.065]</td>
<td>-0.12 [-0.39, 0.15]</td>
<td>-0.25 [-0.52, 0.01]</td>
<td>0.00087 [-0.001, 0.003]</td>
<td>0.0004 [-0.001, 0.002]</td>
</tr>
</tbody>
</table>

There was no significant association between any of the health endpoints and exposure to LG. In fact, all effect estimates were extremely small and with very wide confidence intervals. Overall, there was no evidence of an association between RHI, CRP, IL-6, BCC, or %PMN and exposure to LG.

3.10 Effect Modification by BMI, Age, and Sex

Figure 3-1 Effect modification by sex in the relationship between CRP and PM$_{2.5}$

In order to evaluate whether effects differed by BMI ($\leq 25$ and $>25$), age ($\leq 42$ and $>42$), and sex, stratified analyses were conducted. After stratifying by sex in the CRP and PM$_{2.5}$ mixed model results, it was observed that the effect of PM$_{2.5}$ exposure was only present in males (Figure 3-1). There was a 20.6% (95% CI, 2.62%, 41.7%) increase in CRP levels in men per unit median increase in PM while in women, there
was no evidence of an association (-13.7% (95% CI, -26.5%, 1.42%)). This analysis revealed that the association observed between TRAP and CRP was driven by the effect in males only. All other exposure and outcome pairs were also evaluated for effect modification by BMI, age, and sex; however, there was no evidence of effect modification in any of the mixed models.
4 Discussion

Traffic-related and wood combustion PM are considered to be two major contributors of ambient particle levels in many industrialized countries (de Kok, Driece, Hogervorst, & Briedé, 2006; Saarikoski et al., 2008; Song et al., 2007; Wu et al., 2007). Exposure to TRAP PM occurs throughout the year while WS exposure is greater during colder months. However, it is believed that during cold months, both TRAP and WS contribute to a similar magnitude to the ambient PM concentrations (Glasius et al., 2006; Saarikoski et al., 2008; Song et al., 2007; Wu et al., 2007). Exposure to both sources has been shown to be associated with increased risk of adverse health effects including adverse cardiovascular health outcomes (Naeher et al., 2007; Rückerl, Schneider, Breitner, Cyrys, & Peters, 2011). Despite the overwhelming evidence on cardiovascular effects of PM, there have been very few studies evaluating potential differences between cardiovascular effects of PM from TRAP and WS (Brook et al., 2010). This study is the first study of its kind to directly compare the cardiovascular effects of PM from these two dominant sources of combustion PM.

Overall, HEPA filtration was associated with a 40% decrease in indoor PM$_{2.5}$ concentration. However, there was no conclusive evidence on the relationship between TRAP or WS PM$_{2.5}$ exposure and endothelial function or any of the biomarkers of inflammation. There was some suggestion of an association (borderline significance) between exposure to TRAP PM$_{2.5}$ and CRP levels as the primary endpoint for systematic inflammation in this study. After stratification by sex, the effect was only present in males (statistically significant). There was also some evidence of an association between RHI and absorbance in TRAP homes. Moreover, there was no evidence of an association between IL-6 or BCC and HEPA filtration or PM$_{2.5}$ exposure. All in all, there was a lack of conclusive evidence on the potential differences in cardiovascular effects between TRAP and WS particles.
However, the CRP results may suggest stronger inflammatory effects for TRAP particles and in males.

This is the first study of its kind that has directly compared the potential impact of two combustion sources of PM on cardiovascular health. This study was able to effectively identify individuals exposed to either TRAP or WS PM using detailed spatial air pollution modeling across the sampling region. Comparison of the differences in effect between the two sources provides a unique insight into the similarities and the differences of TRAP and WS PM.

### 4.1 HEPA Filtration Efficiency

With the implementation of indoor HEPA filters, there was a statistically significant reduction of over 40% in PM$_{2.5}$ concentrations with a drop of 36% in TRAP homes and 48% in WS homes. The results in this study were in agreement with a number of other North American studies confirming the effectiveness of HEPA filters. A 2013 review of the literature, the author concluded that overall, studies observed a reduction of over 50% on PM concentrations with HEPA filtration (Fisk, 2013). In a study of a WS impacted community in Canada, Allen et al. (2011) found a reduction of over 60% with the utilization of HEPA filtration. Similarly, in another study of WS impacted homes, there was a 55-65% drop in PM concentration with filtration (Barn et al., 2008)

### 4.2 Mixed Model Conclusions

It should be noted that initially, we intended to include % time at home and % time commuting in the mixed models to account for potential confounding. However, due to lack of data for many individuals and the insensitivity of the analysis to their inclusion, it was decided to remove these variables from the mixed models. Moreover, baseline blood measures were not included or used in any of the mixed models. This decision was made primarily due to the fact that there was no information on exposure metrics prior to the initiation of the study. As a result,
blood measures might have not been representative of what background subclinical indicator levels would have been.

4.2.1 RHI

With RHI as the primary endpoint, mixed model results did not show any significant association between HEPA filtration and endothelial function. In fact, we found no significant relationship between any of PM$_{2.5}$, LG, or absorbance and RHI. Furthermore, the results of the analysis after stratification by home type did not unveil any differences in the effect of filtration on endothelial function between TRAP and WS homes, except for a small association between RHI and absorbance (borderline significance).

Similar to the current study, there have been a number of studies that have evaluated the effect of HEPA filtration on endothelial function with different conclusions. In a study conducted in a WS-impacted community in 2008-09, members of the current study’s research group used a HEPA filter intervention design to investigate the effects of WS PM$_{2.5}$ on endothelial function among healthy adults (Allen et al., 2011). With filtration, the PM$_{2.5}$ concentration dropped from 11.2 µg/m$^3$ to 4.6 µg/m$^3$, which is a 60% reduction. The authors found a statistically significant association between filtration of WS PM$_{2.5}$ and improvements in endothelial function; the use of air filters was associated with a 9.4% increase in RHI. In another study conducted in Denmark, HEPA filtration was used to evaluate the effects traffic-related PM on various markers of cardiovascular health among healthy elderly couples (Bräuner, Forchhammer, et al., 2008). The authors observed a reduction from 12.6 µg/m$^3$ to 4.7 µg/m$^3$ with filtration, a drop of over 60%. They concluded that indoor air filtration was significantly associated with an improvement of 8.1% (95% CI, 0.4%-16.3%) in microvascular function.

In contrast to the above studies, which reported a significant improvement in endothelial function with HEPA filtration, some other studies reported no improvement in endothelial function. In a randomized double-blind crossover
intervention study, HEPA filtration was used to reduce PM$_{2.5}$ levels in mostly smoking First Nations homes to evaluate acute changes in cardiorespiratory health outcomes (Weichenthal et al., 2013). Despite drastic reductions in indoor PM$_{2.5}$ levels from 42.5 µg/m$^3$ to 22.0 µg/m$^3$ by filtration, the authors did not find any significant association between HEPA filtration and endothelial function. The same group of researchers from the study conducted in Denmark recently completed an indoor air filtration study among 48 elderly subjects (51 to 81 years) and evaluated its effect of microvascular endothelial dysfunction (Karottki et al., 2013). The authors did not find any significant relationship looking at filtration as a categorical variable and microvascular function; however, they found an association between PM$_{2.5}$ as a continuous variable and RHI.

There might be a number of explanations for the inability to observe an effect on endothelial function by HEPA filtration and other aforementioned exposure variables. The EndoPAT device used to measure RHI is very particular with regards to exactly following the operating protocol. There were some inconsistencies in the occlusion time after inspecting the PWA output of test, which could have affected the outcome (i.e. under- or over-estimation of RHI depending on the PWA). There has also been some evidence of poor inter-day reproducibility, which might be important when comparing RHI data of the same individual from different days (Liu, Wang, Jin, Roethig, & Unverdorben, 2009). The combination of these two potential sources of error might have affected the results obtained using EndoPAT by either under- or over-estimation of RHI. Another potential explanation for the lack of a significant relationship between RHI and filtration, PM$_{2.5}$, or absorbance in this study could be the relatively low exposure concentrations and small exposure gradients. The indoor concentrations might have been too low to be able to see any measurable improvements in endothelial function by filtration. The small change in PM$_{2.5}$ concentration with filtration could have resulted in a low signal to noise ratio in EndoPAT output, masking small changes in endothelial function.
There have been a number of controlled human WS exposure studies conducted to evaluate the relationship between WS PM and endothelial function. Similar to the results of the current study, most recent studies have failed to find any significant effects on endothelial function. In a randomized double-blind, cross-over study, 20 non-smoking participants were exposed to between 14 and 354 µg/m³ of particles from a well-burning modern woodstove and clean air for 3 hours each session, 7 days apart (Forchhammer et al., 2012). The authors measured endothelial function using endoPAT six hours after exposure but found no effect on endothelial function by exposure to WS PM. In another study, 26 healthy nonsmoking young participants were exposed to 150-200 µg/m³ of fine wood combustion particles generated by a standard woodstove and clean air for three hours each (Pope et al., 2011). Endothelial function was measured using EndoPAT after WS exposure and after exposure to clean air. The authors did not find any evidence of change in endothelial function after exposure to WS PM. It should be noted that these exposures were between twice and over 50 times the exposures our participants experienced in their homes. In addition, these studies introduced much larger concentration gradient between treatment and control session compared to this study, yet failing to find any association between exposure to WS PM and endothelial dysfunction.

4.2.2 CRP

In the current study, we used hs-CRP as a marker of systematic inflammation and cardiovascular health. Numerous studies have shown that hs-CRP can be used as a predictor of future cardiovascular events as a proinflammatory response mediator (Ridker, 2007). Hence, it is recommended as a biomarker for measuring adverse future cardiovascular risk (Jialal, Devaraj, & Venugopal, 2004).

The available evidence in the literature is not entirely consistent regarding the relationship between short-term PM exposure and systematic inflammation (Bräuner, Møller, et al., 2008; Rudez et al., 2009). However, there is a growing body of evidence linking PM exposure with systematic inflammation and adverse cardiovascular health outcomes in general (Brook et al., 2010). In this study, there
was no significant relationship between HEPA filtration and CRP levels in either the overall population or when stratified by home type. When evaluating the effects of PM$_{2.5}$ levels among all participants (both TRAP and WS), we found a non-significant increase in CRP levels per unit median increase in PM$_{2.5}$ in all homes. However, after stratifying by home type, we found a borderline statistical significance (P-value 0.056) for association between CRP and PM$_{2.5}$ levels in TRAP homes only. In fact, there was an 18.4% (95% CI, -0.24%, 40.6%) increase in CRP concentration per unit median increase in indoor PM$_{2.5}$ levels in this subset of homes. After stratification by sex, the effect was only present in males with a 20.6% (95% CI, 2.62%-41.7%) increase in CRP per unit median increase in indoor PM$_{2.5}$ levels. However, there was no association with WS PM$_{2.5}$. There was also no association between CRP and absorbance in this study.

So overall, based on the results from PM$_{2.5}$ models, there was some suggestion of an association between exposure to TRAP particles and systematic inflammation amongst male participants of this study. The results support the a priori hypothesis of a greater impact of TRAP on systematic inflammation compared to WS.

In order to investigate potential gender differences in CRP effect estimates, the mixed models were analyzed by including a gender term in the model. The results indicate that statistically significant CRP effect was restricted to the male subjects in this study. The more pronounced association between CRP and PM in men is consistent with other studies suggesting a link between short-term air pollution exposure and inflammation among male subjects (Briet et al., 2007; Riediker et al., 2004; Rundell, Hoffman, Caviston, Bulbulian, & Hollenbach, 2007; Tan et al., 2000; Törnqvist et al., 2007). There have also been some studies showing an association between CRP and PM$_{2.5}$ in females but the results were less consistent. In a recent systematic review of the literature, Kaptoge et al. (2012) evaluated the evidence from 38 prospective cohorts, with over 166,000 participants, investigating the link between CRP levels and future CHD events. In the pooled analysis of the data from these studies, the author found a statistically significant increase in the risk of future
CVD events associated with CRP levels in males only (Kaptoge et al., 2012). There was also an increase in CVD risk in women however, the effect estimate was much smaller than men’s and non-significant.

Overall, there is a more extensive body of literature investigating the effects of TRAP PM on inflammation as compared to WS studies. In a study of healthy young men, (Riediker et al., 2004) monitored ten highway patrol troopers and PM$_{2.5}$ levels in their cars. In their analysis, there was a 32% increase in CRP levels per 10 µg/m$^3$ increase in PM$_{2.5}$. Dubowsky and colleagues (2006) studied 44 senior citizens with and without conditions related to chronic inflammation (Dubowsky, Suh, Schwartz, Coull, & Gold, 2006). They found significant associations between exposure to TRAP PM and various markers of inflammation including CRP. Moreover, a recent study of 110 traffic policemen in China also found a significant association between exposure to TRAP PM and CRP (Zhao et al., 2013). The current study results are in agreement with the growing body of evidence showing the link between TRAP PM exposure and CRP levels.

The available literature investigating the effects of WS PM on CRP levels is limited and inconclusive at best. There have been very few studies that have linked WS PM to CRP levels. A HEPA filter intervention study by the same research team as the present study in a WS impacted community found a 32.6% (4.4-60.9%) decrease in CRP levels with HEPA filtration. However, they did not observe an association with WS PM$_{2.5}$ levels in homes (Allen et al., 2011). A recent study investigated the inflammatory effects of WS exposure among wildfire firefighters (Hejl et al., 2013). They found borderline statistical significance increase in CRP levels with exposure. In contrast, there have also been a number of other studies, which found no association at all. A short-term controlled exposure study to WS was conducted on 16 healthy non-smokers (20-57 years old) evaluating the effect of WS on systematic inflammation (Stockfelt, Sallsten, Almerud, Basu, & Barregard, 2013). They did not find any significant association between WS PM levels of 146-295 µg/m$^3$ and CRP concentrations.
The current study results further support the *a priori* hypothesis of greater inflammatory effects for CRP in those exposed to TRAP PM compared to those exposed to WS PM. There are at least two possible explanations for this observation. First, the small size of the PM$_{2.5}$ and their large surface area enables them to carry a large number of toxic substance and free radicals present mostly in TRAP PM. This provides an opportunity for the particles to have a biological impact on the cells in the lungs. With increased particle presence in the airways, the phagocytic capacity decreases which leads to their presence for an extended time in the lungs and hence, greater interaction with various cell lines (e.g. epithelial cells) (MacNee et al., 1997). Second, as discussed earlier, the greater abundance of transition metals in TRAP PM compared to WS PM, which can lead to the generation of hydroxyl radicals, oxidative stress, and inflammation (Ghio et al., 1999; Verma et al., 2009) and the greater deposition of traffic particles in the lungs could further explain these results (Löndahl et al., 2008; Löndahl et al., 2009).

Finally, as mentioned above, there was no relationship between HEPA filtration and CRP while there was a suggestion of an association between TRAP PM$_{2.5}$, as a continuous variable, and CRP levels. These findings could be possibly explained by the fact that some homes were included in the study during warmer month and hence, there was a greater probability of having open windows while sampling. As a result, there might have been reduced HEPA filter effectiveness, which cannot be captured by the binary intervention variable (i.e. HEPA/no HEPA). However, such a discrepancy in filtration efficiency can be captured by the continuous PM$_{2.5}$ concentration variable. As a result, this might explain the reason behind finding a suggestion of an association between PM$_{2.5}$ and CRP but not HEPA and CRP.

### 4.2.3 IL-6

As one of the secondary endpoints of systematic inflammation, IL-6 was also included in the analysis. IL-6 is known to be one of the cytokines involved in initiating acute phase inflammatory response in the body by promoting the
synthesis of various proteins including CRP (Gabay & Kushner, 1999; van Eeden et al., 2005).

There have been conflicting studies investigating an association between IL-6 as an inflammatory marker and the risk of cardiovascular events. In a prospective cohort study, 2,225 elderly participants without baseline CVD were enrolled in the study. Upon follow up and adjusting for potential confounders, IL-6 was found to be significantly associated with increased risk of CHD events (27%-86% increase) per IL-6 SD increase (Cesari et al., 2003). In a nested case-control on 317 participants, (Luc et al., 2003) followed subjects for five years, recording initial CHD events. They concluded that IL-6 levels were significantly associated with adverse coronary outcomes. However, a recent large-scale prospective cohort study followed over 51,000 individuals with no baseline cardiovascular health issue for up to 8 years (Pai et al., 2004). During the follow-up period, they identified 249 women and 266 men who developed cardiovascular events. Blood samples were collected biennially during the follow-up period and analyzed for various inflammatory biomarkers. After adjusting for potential confounders, the authors concluded that there was no association between adverse cardiovascular events and IL-6 levels.

The results of the analysis were not as hypothesized for the relationship between HEPA filtration and IL-6 levels. There was no significant relationship between IL-6 and any of the exposure variables that were evaluated. Most effect estimates were very small with wide confidence intervals rejecting an association.

Despite the expectation of the same level of association between CRP and PM$_{2.5}$ exposure due to the physiological link between IL-6 and CRP, the results seem to be in agreement with a number of other studies which failed to find any significant effects of TRAP and WS PM on IL-6 levels in the body. In a recent controlled exposure study, participants were exposed to 146-295 µg/m$^3$ WS PM (Stockfelt et al., 2013). The authors found no relationship between exposure to WS and CRP or IL-6 in participants. This was contrary to their previous exposure study where they
used higher doses of WS PM and found a decrease in IL-6 with exposure to filtered air (Barregard et al., 2006a). In a filtration based intervention study in Denmark, 21 elderly couples participated in a randomized, double-blind, crossover study investigating the relationship between HEPA filtration and various markers of inflammation (Bräuner, Forchhammer, et al., 2008). They found no significant change in IL-6 levels with HEPA filtration of TRAP PM. Moreover, (Jacobs et al., 2010) recruited 38 volunteers that cycled in real traffic and in a laboratory with filtered air. Their results were inconclusive with regards to exposure to TRAP PM$_{2.5}$ and IL-6 levels.

### 4.2.4 BCC and %PMN

Band cells are immature polymorphonuclear leukocytes (PMN) produced in the bone marrow. Increases in BCC is an indication of stimulation of the immune system leading to an increased release of granulocytes in the bone marrow (Tan et al., 2000). There is evidence that exposure to high levels of ambient PM can potentially lead to a spike in the release of band cells (van Eeden et al., 2005). In a study of high level WS exposure, healthy non-smoking firefighters (17-60 years old) with no chronic medical condition or prescription medication use were recruited (Swiston et al., 2008). During wildfire episodes, the firefighters were exposed to PM levels as high as 2,000 µg/m$^3$. This study found a statistically significant increase in BCC and PMN following fire fighting, which could be indicative of systematic inflammation. In another study, (Sakai et al., 2004) followed 39 research expedition members from Japan to Antarctica for several months and then back to Japan. They found PM levels to be <1% of that measured in Japan because of less use of fossil fuels in Antarctica. The authors found a significant association between PM exposure and BCC/PMN with reductions after moving to Antarctica and increases after moving back to Japan. Despite the available evidence in the literature, there was no evidence of an association between HEPA filtration and BCC as %PMN in the current study. Furthermore, there was no significant relationship between PM$_{2.5}$ and %PMN. However, the effect estimates were in the hypothesized direction with increases in %PMN per unit median increase in PM$_{2.5}$ levels, though not statistically significant.
and very small. The same trend was true when looking at the relationship with absorbance and LG.

Overall, the results of this current study are not in agreement with the available literature discussed earlier. There was no significant relationship between BCC/%PMN and various exposure measures. The subjects in most studies that found an association between the two variables were exposed to PM levels up to 200 times greater than what was measured in the current study (Sakai et al., 2004; Swiston et al., 2008). The fact that the exposures were very low in this study could be a valid explanation for the inability to observe an effect by TRAP and WS exposure variables on BCC/%PMN.

### 4.3 Conclusions

All in all, this study suggests an association between TRAP PM$_{2.5}$ exposure and CRP levels in male participants but no associations with IL-6, BCC, or %PMN. The value of “negative” results of this study should not be underestimated, as they could be valuable for determining future research direction evaluating the effects of TRAP and WS PM and also interventions on cardiovascular health. It should be noted that the baseline PM concentration was relatively low with small exposure gradients after HEPA filtration. Moreover, the population evaluated was relatively young and healthy without any type of CVD risk factors, medications or health conditions affecting inflammation. In such a context, the findings with regards to the effect of PM exposure on CRP in TRAP homes can be considered a valuable addition to the scientific literature. In addition, the results are partially consistent with the a priori hypothesis that there will be a greater impact on cardiovascular health in those exposed to traffic-related PM$_{2.5}$, however, we observed this impact only amongst male participants. The results partially support the hypothesis that HEPA filtration can be effective in reducing indoor PM$_{2.5}$ concentrations with some suggestion of an effect on systematic inflammation marker concentrations in the body in TRAP homes, among males only.
4.4 Significance of Study

To our knowledge, this was the first study to directly compare the potential cardiovascular effects of WS and TRAP particles directly. There has been some evidence on the effectiveness of HEPA filters as an intervention for traffic-generated particles but they are from studies conducted in Europe. Since a greater proportion of vehicles use diesel as fuel in Europe compared to North America, it might not be practical to extrapolate their results into a North American setting. This study provides a better insight into the use of HEPA filters in North America as an intervention for traffic-generated PM exposure. Furthermore, the crossover design of this study neutralized potential confounding bias since individuals serve as their own control.

Being the first study comparing the cardiovascular effects of PM exposure produced from TRAP and WS, this study is valuable for risk assessment of these two common sources of PM. The quantitative evaluation of the effectiveness of HEPA filtration as an intervention for the reduction of PM exposure from these two sources can assist us with future decision and policymaking for reducing exposure to PM. Future research on the health effects of PM from RWC will better enable us to develop air quality management strategies.

4.5 Strengths

In this study, several recommended approaches in the understanding of PM source impacts were addressed (WHO, 2007). The effect of PM from sources other than TRAP, assessed the contribution of different exposure sources to population exposure, using specific health markers other than general mortality and lung function, and finally, evaluating the effects of air pollution reduction on health outcomes were addressed by using a novel semi-experimental study design. Controlled laboratory experimental exposure studies generally restrict exposure parameters to a specific air pollutant at very high concentrations or certain sources such as gasoline exhaust, while this is not the case in real world exposure settings.
(Strak et al., 2012). With a semi-experimental design, the test subjects were exposed to real-life ambient air pollution with contrasting PM exposure sources and concentrations. This advantage is valuable for the applicability of this study's results to the general population.

4.6 Limitations

As with any other study, the limitations of the current study should be considered. As shown in this study, PM$_{2.5}$ concentrations were very low in the sampling region. With such a low PM$_{2.5}$ concentration, the gradient introduced with HEPA filtration was also very small compared to other similar studies. As a result, the concentration gradient might have been too low to see any measurable change in the health variables of interest.

In this study, RHI was used as the primary outcome for assessing cardiovascular risk of exposure to PM$_{2.5}$. However, the available literature has not been entirely consistent on the extent that EndoPAT results agree with other well developed, clinically used methods (e.g. endothelium-dependent brachial artery flow-mediated dilation). Of the nine available studies comparing the two methods, six found statistically significant weak to moderate correlation (Dhindsa et al., 2008; Heffernan, Karas, Mooney, Patel, & Kuvin, 2010; Kuvin et al., 2003; Kuvin, Mammen, Mooney, Alsheikh-Ali, & Karas, 2007; Onkelinx et al., 2012; Schnabel et al., 2011), while three found no significant correlation between endoPAT results and flow-mediated dilation method (Aizer et al., 2009; Dickinson, Clifton, & Keogh, 2011; Hamburg et al., 2011). Despite these differences, there have been suggestions that RHI is able to predict adverse cardiovascular health outcomes (Rubinshtein et al., 2010). It should be noted that these studies used different flow mediated dilation protocols, which makes drawing any sort of conclusion on the reliability of endoPAT very difficult; there is a need for more standardized research to enable us to conclusively determine the correlation between clinical methods and endoPAT. Meanwhile, there is a chance that such inconsistencies might have affected the evaluation of endothelial function in participants.
It should also be noted that many different mixed models were used in this study. In addition, each of the mixed models were also analyzed after stratifying for various variables. As a result, such a great number of models might have increased the chances of finding an association due to chance only (e.g. PM and CRP in TRAP homes among males).

Moreover, 2 to 31 participants were excluded from different mixed models in the study due to missing or flawed data for different variables (e.g. RHI, CRP, PM$_{2.5}$, etc.). However, it should be noted that the comparison of health and exposure outcomes between the “included” and the “excluded” participants did not show any significant differences between the two groups.

In order to identify homes in high TRAP PM areas, the spatial model used NO$_x$, which is a gas and not a particle, as a surrogate for TRAP. Due to the fact the gas concentration gradient as one moves away from traffic source is not the same as PM gradient, these areas may not actually be high in traffic-related PM. While there are not big gradients in PM mass, there are somewhat more pronounced gradients in some PM measures such as black carbon. In addition, since most of the TRAP homes were in close proximity to major roads or highways this limitation might have had minimal effect on the categorization.

Despite the benefits of the crossover design of this study in minimizing the effects of within-participant characteristics of the analysis, treatment carryover effects were of concern. However, the carryover effect between HEPA and no HEPA treatment periods was eliminated by using a 7-day period for each treatment. According to the available literature, the half-life of CRP is approximately 19 hours (Gabay & Kushner, 1999). There have also been reports of a lag time of 2 days for seeing the effects of HEPA filtration on microvascular endothelial function (Bräuner et al., 2008; Karottki et al., 2013). Considering these findings, it is expected that there were minimal carryover effects at the end of each 7-day treatment session.
The initial goal was to enroll a total of 100 participants, 50 in each exposure group. However, due to the shorter length of the wood use season during the colder months of the year compared to traffic-related sampling, only 83 participants were enrolled with 29 from WS homes and 54 from TRAP exposed homes. As a result, this study did not have sufficient statistical power to test for small differences in HEPA filtration effects between the two exposure groups. With the initial expected number of participants and an expectation to find a large difference between TRAP and WS PM exposure effects, the mixed models had high statistical power. Considering the fact that the expected number of participants was not met, this study might have failed to measure small differences between the two groups due to lack of sufficient statistical power. However, it should be noted that the probability of change in the direction of effect is minimal considering the current trends presented in the results section.

Although electrical current meters were utilized to ensure HEPA filtration use during this study, there are still some uncertainties with regards to proper use of these devices due to the different output settings present on the device. Despite this shortfall, most homes had reductions in PM$_{2.5}$ levels with filtration reducing the likelihood of a large effect on the study. Moreover, there was a possibility for individuals to open the devices, check for filter presence, and disturb blinding; however, since participants were not aware that there will only be placebo filtration during one of the weeks, there was no reason to be concerned about this issue.

Finally, while it was not possible to record air pollution exposure in other microenvironments outside the homes, where the participants spend about 25% of their time. This should not be a major source of error affecting the effectiveness of HEPA filtration, due to the crossover nature of this study. In addition, the time-activity patterns were very similar between the HEPA and no HEPA weeks further alleviating any concern.
4.7 Suggested Future Research

To further evaluate the results of this study and to extend the conclusions, more research is needed. Future studies investigating the effects of HEPA filtration on cardiovascular health could focus on homes with higher levels of PM$_{2.5}$. Higher levels will assist with producing a greater concentration gradient using filtration devices, which might lead to more measurable differences. Using the same novel approach employed in this study by utilizing filtration devices and evaluating more than one source of PM in the same study population could be useful in testing the differential impacts of specific PM sources without removing participants from their residences.

At such low PM concentrations in the developed world, the change in various health outcomes could be very small. Hence, the recruitment of more participants could prove useful in increasing the statistical power of the study to detect smaller differences in effect between TRAP and WS PM$_{2.5}$. Finally, the participants in this study were relatively young and healthy. This might limit the generalizability of this study to the general population. It might be valuable to study the effects of HEPA filtration among vulnerable populations (e.g. diabetics) as they are the group at the greatest risk of developing adverse health effects from exposure to PM$_{2.5}$ (Sacks et al., 2011).

4.8 Implications on Public Health

With the mounting evidence on the effects of exposure to PM$_{2.5}$ from combustion sources on cardiovascular health, there is an immediate need to reduce public exposure. To achieve such a goal, the decision making bodies will need to have an understanding of the sources of exposure and the potential differential effects that they might have on health. While changes are being brought about at the general population and policy levels, steps could be taken at individual level to reduce exposure to PM$_{2.5}$. Although there was no evidence that HEPA filtration reduced health impacts in the current study, there was some suggestion of worsening systematic inflammation with TRAP PM$_{2.5}$ exposure. Moreover, this study along with
other available literature have suggested a potential for HEPA filtration to reduce indoor TRAP and WS PM$_{2.5}$ concentrations. Considering the toxicological and biological plausibility of a link between PM$_{2.5}$ and adverse health effects, the utilization of HEPA filtration at homes and workplaces can be an inexpensive and yet effective means of reducing the effects of air pollution on cardiovascular health and other health effects. The effect of HEPA filtration might be relatively small at an individual level but when evaluating the effects at a population level, there is a potential for substantially reducing risks associated with exposure to PM$_{2.5}$. Nevertheless, it should be kept in mind that the most important aspects of reducing air pollution exposure is through targeting the source of pollution and designing interventions at the source. Meanwhile, HEPA filtration could be evaluated as a potentially viable option.
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APPENDICES
APPENDIX I: INVITATION LETTERS
Cardiovascular Effects of Aerosols in Residences Study (CLEAR)

http://www.sfu.ca/clearstudy/

Dear Resident:

I am working with a team of researchers from Simon Fraser University (SFU) and the University of British Columbia (UBC) who are investigating the health effects of air pollution. I am writing to invite you to participate in a study currently underway. Adults (19 years or older) residing in Greater Vancouver, BC may be eligible to participate in the study. Unfortunately, homes with residents who smoke are not able to be considered for participation.

The study involves air monitoring inside and outside your home and the use of portable air cleaners to determine their effectiveness regarding improved indoor air quality and improved health. In order to measure health improvements we will be collecting blood samples (three times) and conducting a non-invasive test of vascular function (twice). All air sampling will be conducted over 2 consecutive 7-day periods; health measurements will be done at the beginning of sampling, halfway through sampling and again at the end of the sampling period. At the initial visit, 2 technicians will visit your home. The environmental technician will setup the air monitoring equipment inside and outside your home and gather some information on your home (age, size, type of heating system, etc.); the health technician will complete a short questionnaire on your health and perform the first blood
draw. In addition to the air monitoring equipment, 2 portable high efficiency particulate air (HEPA) filters will be installed in your home, one in your bedroom and one in your main living room. These devices are quiet, require no maintenance, and will not affect your daily routine.

After the initial visit, the air monitoring equipment will run unaided until the end of the first 7-day period when both technicians will visit your home again. At this second visit, the environmental technician will perform maintenance checks on the equipment, and the health technician will perform a second blood draw and also perform a non-invasive test of your vascular function. The vascular function test involves having a blood-pressure cuff on one arm, and a small sensor on two fingers. The test lasts about 20 minutes and should not cause any discomfort. We will also ask you questions about any health symptoms you may have experienced during the first week of sampling.

Data collection is currently underway and will continue until approximately August, 2012. Your commitment will be approximately 4 hours in total. Sampling will be conducted by fully trained study technicians and will be scheduled to start and end on a weekday morning. All 3 visits will be conducted in the morning, as it is important that the health measurements be performed before you’ve had breakfast or any caffeine. The technicians will work with you to find a time convenient for you to install the equipment and perform the health sampling.

Finally, while the equipment is running, we ask that you keep a simple diary of time spent at home and of any possible pollution-generating activities (cooking, vacuuming, etc.). A diary will be supplied for this recording.
The sampling instruments collect information only on air quality and run unaided but do require a small amount of power to run. Beyond the activities described above, your participation in this study should not interfere with your daily routine. All personal information collected will remain completely confidential and will be securely stored according to University policy. No one other than the study team members will have access to the data collected, and individuals are never named or identifiable in any reports or publications.

In order to assist with the inconvenience of participating in this study, you will receive an honorarium. We are able to enroll 1 or 2 subjects per home, so if there is a second adult in your home who is interested and eligible to participate, they would also receive the honorarium.

If you are interested in participating, or would like further details about the study, equipment used or any of the procedures, please call Barbara Karlen at 778-782-9324 or email clear@sfu.ca. Further information is also available on the study website: www.sfu.ca/clearstudy. Alternately you can contact me at the number or e-mail address listed below.

Thank you for your time and for considering participating in this important research.

Sincerely,

Dr. Ryan Allen Assistant Professor
Faculty of Health Sciences Simon Fraser University (778) 782-7631
allenr@sfu.ca
APPENDIX II: PARTICIPANT SCREENING
Participant screening (to be done by phone)

Name: ___________________________ Date: ____________

**First, give a description of the research study and what is involved in participating, specifically:**
- early morning, weekday sampling session start and end;
- 3 blood samples;
- fasting before all 3 blood samples and vascular function measurement – first thing in morning;
- instruments running indoors and outdoors for two consecutive 7-day sessions;
- home and symptom questionnaires;
- activity diary.

If potentially interested, ask the following eligibility screening questions:

1. **Home address (with postal code):** ____________________________

2. **What type of building do you live in?** ____________________________
   a. If apartment or condo, what floor do you live on (1st floor = ground level)? _______

3. **Is there a secure outdoor location close to your home (such as a yard, patio, or balcony) where we could place our outdoor air pollution sampling equipment? Yes No**
   a. If yes, does this location have an accessible electrical outlet? Yes No

4. **Do you smoke?** Yes No

5. **Are there any smokers residing in your home? Yes No**

6. **Have you been diagnosed by a physician/dentist with any of the following? Check if yes, and for those that apply, ask if they currently take any medication for the condition and which medication is taken.**
   
   † **COPD (chronic obstructive pulmonary disease/chronic bronchitis/emphysema) Medication:** ____________________
   
   † **asthma**
   
   † **diabetes**
   
   † **heart disease (including coronary heart disease, stroke, myocardial infarction (heart attack), heart failure, angina, arrhythmia)**
     Medication: ____________________________
hypertension
    Medication: ________________________________

arthritis
    Medication: ________________________________

gum disease
    Medication: ________________________________

7. Have you been diagnosed with any other current conditions?
   Describe: ________________________________

8. Have you had surgery in the last 6 months?   Yes   No   Date: ______________

9. Are you pregnant?   Yes   No

10. Do you currently have an infection of any kind (including colds)?
    Yes   No Describe: ___

11. Do you currently take any other regular medications?  Yes   No
    Please list: ________________________________

12. What is your current weight?   ______________

13. What is your height?   ______________

14. Have you traveled out of the region recently? Dates (from – to) : ______________
    Where: ________________________________

15. Do you work or regularly volunteer outside the home?  Yes   No  (IF NO SKIP TO 16)

   a. If yes, how many hours per week do you typically work/volunteer outside the home? ________________________________

   b. what is your occupation / volunteer activity? ________________________________

   c. are you regularly exposed to dust, exhaust, or smoke at work/volunteer?
      Yes
      No

   i. If yes, please describe: ________________________________
d. how do you usually commute to work / volunteer location? ______________________

e. how much time per day do you typically spend commuting to and from work/volunteer?
   __________(enter total round trip commuting time)

16. Do you currently use a wood-burning appliance in your home?  Yes  No (IF NO
   SKIP TO 17)

   a. If yes, what type of appliance do you have?
      i. Fireplace
      ii. Conventional wood stove
      iii. Insert
      iv. Certified wood stove
      v. Pellet stove

   b. do you tend the fire?  Yes  No

   c. approximate proportion of fire-tending that you do: ______________________

17. What is your year of birth? ______________________

18. Is there another adult in your household who may be interested in participating?  Yes
   N

   Would you ask them whether they are interested in speaking to me about this study and
   whether they are available to speak to me now?

   If they are not available now, would you please pass on the intro letter to them and ask them to
   phone me if they are interested in participating or would like more information.

   do you tend the fire?  Yes  No

   a. approximate proportion of fire-tending that you do: ______________________

19. What is your year of birth? ______________________

20. Is there another adult in your household who may be interested in participating?  Yes
   N

   Would you ask them whether they are interested in speaking to me about this study and
   whether they are available to speak to me now?

   If they are not available now, would you please pass on the intro letter to them and ask them to
   phone me if they are interested in participating or would like more information.
Contact information:

Phone number: (H) __________________ (C) __________________

Best time to contact: __________________

Best to call: home / cell
Email: _____________________________

End the call with:

“Thank you for your interest and your time; we'll be reviewing your eligibility for the study and will be back in touch with you within 2 weeks to let you know whether we are able to enroll you in the study”.

OFFICE USE ONLY:

□ Not Acceptable

Acceptable

□

Priority 1 recruit or,
Priority 2 recruit

Call back date: __

Scheduled for: __
APPENDIX III: INFORMED CONSENT
SUBJECT INFORMATION AND CONSENT FORM

Cardiovascular Effects of Aerosols in Residences Study (CLEAR)

Principal Investigator:
Dr. Ryan Allen  
Faculty of Health Sciences Simon Fraser University Phone: (778) 782-7631  
E-mail: allenr@sfu.ca

Co-Investigators:
Dr. Michael Brauer  
School of Population and Public Health  
The University of British Columbia

Dr. Stephan van Eeden  
Dept. of Internal Medicine & Respirology  
University of British Columbia

Dr. Christopher Carlsten  
School of Population and Public Health  
The University of British Columbia

The purpose of this study is to evaluate the health benefits of high efficiency particulate air (HEPA) filters and to compare the cardiovascular health effects of two major particulate matter sources (traffic-related air pollution & residential woodsmoke emissions).

This study will be conducted in the Vancouver and surrounding area commencing at the start of the 2011/12 winter heating season and will continue until approximately 100 people are enrolled.

Introduction
You are being invited to participate in this study because you live in a community in greater Vancouver, BC that has air pollution originating from traffic emissions and/or from residential woodsmoke.

Your participation is voluntary
Your participation in this study is entirely voluntary. If you decide to take part in this study, you are still free to withdraw at any time without giving any reasons for your decision. We ask that you please take time to read the following information before you decide.

Who is conducting the study?
This study is being conducted by researchers at Simon Fraser University, and the University of British Columbia and is being funded by the Canadian Institutes of Health Research.

**Background**

Air pollution from a variety of sources can negatively affect health. HEPA filters are expected to significantly reduce indoor levels of airborne particles and to improve health.

The objectives of this study are to: 1) quantify the relationship between low-level exposures to combustion-derived PM air pollution and subclinical indicators of cardiovascular disease risk; 2) evaluate and compare the impact of two exposure reduction approaches – HEPA filters and a community woodstove exchange program (underway in the Smithers and Telkwa areas) – on reductions in exposure and measurable improvements in sensitive subclinical cardiovascular health indicators among healthy adult participants; and 3) compare the relative impact of HEPA filtration for two major PM sources (traffic and residential wood combustion) on these indicators.

**What is the purpose of the study?**

This study will examine the health effects of exposure to different sources of air pollution in adults, and assess the effectiveness of portable HEPA filter air cleaners toward improving indoor air quality and improving health.

**Who can participate in the study?**

To participate in this study, you must be at least 19 years old and live in one of the targeted areas in the Vancouver and outlying areas.

**Who should not participate in the study?**

Smoking will affect the air quality inside the home, and therefore households with residents who smoke must be excluded from this study. We may exclude individuals with a prior diagnosis by their doctor of asthma, chronic obstructive pulmonary disease (COPD), heart disease, diabetes, or hypertension. We may also exclude individuals living in neighbourhoods previously identified as being influenced by air pollution sources other than those of interest in this study.

**What does the study involve? Overview**

The total sampling time is 14 days. Two back-to-back air pollution sampling sessions will take place in your home and will last 7 days each. The two consecutive 7-day sessions will start and end on a weekday morning, with a total of 3 visits during that time from the study technicians. Sampling sessions will be scheduled at a time convenient for you, when you have been free of any colds or other infections for at least 2 weeks.

For the duration of the sampling session, air monitoring instruments and HEPA filters will be running in your home. At the start of sampling (visit one), sampling instruments will be set up, and you will be interviewed about your health status and characteristics of your home; you will also be asked to provide a small blood sample. At visit 2 and visit 3 (the end of sampling) maintenance on the equipment (equipment removal at visit 3) will be performed. Also at visits 2 and 3, repeat blood samples will be drawn, and the blood vessel health test will be performed. In all, 3 blood draws will be done, and 2 blood vessel health tests will be performed.
Here is a list of the specific procedures that will be included if you decide to join this study:

At visit one:

The environmental technician will set up a portable air cleaner in your bedroom and in the main common room (a room other than the kitchen) of your home. He or she will also set up air quality monitoring equipment in the main common room and in a secure outdoor area. This equipment will measure fine particulate matter (PM$_{2.5}$) in the air as well as an odourless gaseous air pollutant, carbon monoxide (CO). The equipment is designed to operate quietly and unobtrusively and presents no known risks to the occupants of the home. In total, the equipment will take up a 1 meter x 1 meter space and technicians will work with you to locate it to minimize any disruptions. The equipment will need to be plugged into an electrical outlet in each of those areas;

The environmental technician will need access to your home for approximately one hour at visit one for the installation, and you will need to be present to answer some questions about your home’s characteristics (age, building materials, heating system etc.);

The medical technician will be present to ask you some questions about your health status and take a blood sample (approximately 15 ml, or 1 tablespoon) from your arm. This visit will be made as early as convenient for you in the morning.

At visit two (7 days after visit one):

The technicians will need access to your home for approximately 45 minutes to perform maintenance on the air samplers;

During this visit, a non-invasive test of the health of your blood vessels will be performed (vascular function). This involves having a blood-pressure cuff on one arm and a small sensor on two fingers. The test takes approximately 20 minutes and should not cause any discomfort. Since this measurement requires you to fast for 5 hours before the measurement, this test will be made as early as convenient for you in the morning. The second blood sample will be collected at this time.

At visit three (7 days after visit 2):

The technicians will return to your home a final time to shut off and remove all equipment;

The final blood vessel health test and collection of the final blood sample will be performed. The visit will take approximately 45 minutes to 1 hour, and as with visit two, will be scheduled for as early as convenient in the morning.

With the exception of fasting prior to the blood draws and blood vessel tests, you and other residents should engage in normal activities during the monitoring session. You will be asked to keep a simple log of locations and activities (at home, at work, use of woodstove, cooking, dusting, etc.) for each sampling period. You will also be asked to complete a brief questionnaire about health irritation symptoms you may have experienced during the sampling session. You do not need to respond to any questions that you are not comfortable answering.

The total amount of direct contact time with study technicians required for you to participate in the study is about 3.5 to 4 hours.
All blood samples and blood vessel tests will be identified by research code only; no personally identifying information will be used.

If you agree to being contacted in the future, we may invite you to participate in a follow-up study. You may indicate your willingness to be contacted for future studies at the end of this consent form.

**What are the possible harms of participating?**

There may be some minor discomfort or bruising on your arm at the site of the blood collection and you may experience some lightheadedness and/or fainting. As with any blood sample collection, there is a very small risk of infection at the site of the collection. There are no risks involved with the measurement of vascular function. As both the blood test and the vascular function measurement requires that you do not eat in the 5 hours before the test, this may cause some temporary discomfort due to hunger; we will schedule all procedures as early as convenient for you in order to minimize this disruption.

There are no risks involved with the air pollution sampling. All sampling involves measurement of compounds normally present in indoor and outdoor air. There are no risks involved with the air cleaner, which filters out fine particles from the air.

Participating in this study may cause some inconvenience for yourself and other members of your household, but technicians will work with you to minimize these impacts.

**What are the possible benefits of participating in this study?**

You will receive a summary of the measurements made in your home at the end of the study. You may also benefit from learning more about air quality and the effectiveness of HEPA air cleaners toward improving indoor air quality.

**What happens if you decide to withdraw your consent to participate?**

Your participation in this research is entirely voluntary. You may withdraw from this study at any time. If you decide to participate and then decide to withdraw at any time during the course of the study, your samples will have their ID number removed and they will be discarded according to standard laboratory procedures. There will be no penalty or loss of benefits to which you are otherwise entitled. If you wish to withdraw from this study, please contact the study coordinator, at the number listed at the end of this document.

If you choose to enter the study and then decide to withdraw after the study has been completed, all data collected about you during your enrolment in the study will be retained for analysis. All data and personal samples collected will be governed by the Personal Protection and Electronic Documents Act (PIPEDA) and also by the SFU Office of Research Ethics Policy R20.01

**After the study is finished**

At the end of the study, a summary of your personal results will be sent to you by mail to your home address.

**Possible cost of participating in the study**

The equipment will need to be plugged into an electrical source and will use a small amount of electricity.
Payment to you for Participating

To assist with the inconvenience of your participation in this study, you will receive an honorarium of $250 upon completion of the two week sampling session. If you do not complete the sessions, the payment will be pro-rated to the amount of time you participated.

Will my taking part in this study be kept confidential?

Your confidentiality will be respected. No information that discloses your identity will be released or published without your specific consent to the disclosure. All samples and tests will be identified by a code only; personal identifiers will be removed. Participants Master File Key (the document with your name and individual code) are kept in a locked cabinet in a secure office at SFU. However, no records which identify you by name or initials will be allowed to leave the Investigators' offices. All documents are kept at SFU for the purpose of monitoring the research for a period of 5 years.

Whom do I contact if I have questions about the study during my participation?

If you have any questions or desire further information about this study before or during participation, you can contact the study technicians, (T.B.D.), the study coordinator, Barbara Karlen at 778.782.9324 (cell: 604.839.2341), or the principal investigator Ryan Allen at 778.782.7631

Whom do I contact if I have any questions or concerns about my rights as a subject during the study?

If you have any concerns about your rights as a research subject and/or your experiences while participating in this study, contact:

Dr. Hal Weinberg, Director, Simon Fraser University Office of Research Ethics at <hal_weinberg@sfu.ca> or 778-782-6593

Conflict of Interest

There are no known conflicts of interest on the part of the study investigators or the study sponsors (CIHR: Canadian Institutes of Health Research).

Subject consent to participate

I have read and understood this consent form. I have had sufficient time to consider the information provided and to ask for advice if necessary;
I understand that my participation in this study is entirely voluntary and that I may refuse to participate or withdraw from the study at any time without any consequences;
I understand that all of the information collected will be kept confidential and will only be used for scientific objectives;
I understand that I am not waiving any of my legal rights by signing this consent form;
I have been told that I will receive a dated and signed copy of this consent form.

My signature below indicates that I consent to participate in the Cardiovascular Effects of Aerosols in Residences (CLEAR) Study:

And, if checked below, that I consent to future contact for follow-up.

Study personnel may contact me about future follow-up research studies
<table>
<thead>
<tr>
<th>Printed Name of Subject</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Printed Name of Witness</td>
<td>Signature</td>
<td>Date</td>
</tr>
<tr>
<td>Printed Name of</td>
<td>Signature</td>
<td>Date Principal Investigator</td>
</tr>
</tbody>
</table>
APPENDIX IV: HEALTH AND EXPOSURE REPORT
Thank you for participating in the Cardiovascular Effects of Aerosols in Residences (CLEAR) Study
October 27th, 2012

Dear <first name>,

Thank you for participating in the Cardiovascular Effects of Aerosols in Residences (CLEAR) Study. We sincerely appreciate your willingness to allow us into your home, permit air sampling, and participate in blood draws and blood vessel measurements. We are also grateful for your patience in awaiting these results; the numerous analyses in multiple laboratories take time and results are most meaningful when we can report your measurements in the context of all study participants’ results.

STUDY OVERVIEW:
As you will recall, this survey had two components: a health component and an air monitoring component. We collected participants’ blood on three occasions and measured blood pressure and the health of participants’ blood vessels on two occasions; in addition, we measured the air (particulate matter) inside and outside participants’ homes over a two-week period. Together these measurements are helping us understand the cardiovascular health effects of air pollution and the potential benefits of using high efficiency particulate air (HEPA) filters indoors.

THIS REPORT:
This report shows your personal (physiological) results from both testing sessions and results from the environmental sampling conducted inside your home (with outdoor measurements used for a comparison). Physiological results reported include C-reactive protein (CRP) in your blood, an indicator of inflammation, and endothelial function, an indicator of blood vessel health. For both measurements, we are also providing some information to help you interpret your results. Other measurements in blood are considered experimental; results for those tests are not included here as there are no expected “normal” values for comparison. Please feel free to contact us if you are particularly interested in any results not reported here.

Environmental results reported include PM_{2.5} (particulate matter of 2.5 microns or smaller in diameter), levoglucosan (a marker of wood smoke particulate matter), hopanes (an organic marker for traffic-related particles), and infiltration efficiency (the fraction of the outdoor particulate matter that makes its way inside your home). All environmental measurements were taken over two 1-week (7-day) periods. For one of the 7-day periods, a HEPA filter was in place in the air cleaner housing unit; for the other 7-day period the air cleaner was operated without a HEPA filter installed. Whether the HEPA filter was in place during the first or second week of sampling was determined randomly.

At the same time as your indoor sampling, we collected environmental data outside of your home. In addition to giving us measurements of the amount of particulate matter in the atmosphere around your residence, this information is used to determine the infiltration rate for your home.

GENERAL STUDY FINDINGS:
Our analysis confirmed that the HEPA filter air cleaners do improve overall air quality inside homes. On average, the use of HEPA filters resulted in a XX% reduction in levels of particulate air pollution (from a variety of sources including traffic, woodburning, cooking, etc.) indoors. In addition, we found that the use of HEPA filter air cleaners resulted in improved blood vessel health and reduced levels inflammation. Although the clinical significance of these relatively small changes is not clear, it does suggest that the use of HEPA filter air cleaners in this setting can reduce some negative impacts of exposure to air pollution.

YOUR PERSONAL MEASUREMENTS:

You supplied blood samples on three occasions and underwent a blood vessel health measurement (endothelial function) on two occasions. One 7-day sampling session measured with the HEPA filter in place and the other 7-day sampling session measured without the filter in place.

As mentioned on the previous page, most of the analyses on the blood are experimental; therefore, only the tests for CRP in blood and your blood vessel (endothelial) function are reported here. Please note that for CRP a higher value indicates greater cardiovascular risk, while for the blood vessel measurements a higher value indicates healthier vessels.

Cold/Flu symptoms present at the time of your tests: <cold/flu – yes/no> Blood Pressure at visit 1: <bp visit X>
Blood Pressure at visit 2: <bp visit 1> Blood Pressure at visit 3: <bp visit 2>

<table>
<thead>
<tr>
<th>TEST</th>
<th>With HEPA Filter in place</th>
<th>Without HEPA Filter in place</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP* (mg/l)</td>
<td>&lt;hepa 1 CRP&gt; XXXX-XXXX</td>
<td>&lt;hepa 0 CRP&gt; XXXX-XXXX</td>
</tr>
<tr>
<td>Endothelial Function**</td>
<td>&lt;hepa 1 endo&gt; XXXX-XXXX</td>
<td>&lt;hepa 0 endo&gt; XXXX-XXXX</td>
</tr>
</tbody>
</table>

* C-Reactive Protein (CRP) measured in blood is a marker of inflammation in the body, and is used as a general indicator of cardiovascular disease risk. Higher values indicate more inflammation. It is important to note that this measurement is sensitive to whether or not you had a cold, flu or other infection during this time and the results should therefore be interpreted cautiously. The following chart will help you to see how your results for CRP can be interpreted. We suggest that you discus any elevated measurements with your physician:

1 mg/l = low risk
1 - 3 mg/l = moderate risk
3 mg/l = high risk
10 mg/l = consult your physician for a repeat test

** Endothelial Function is a test of the health of the endothelium - a layer of cells that line blood vessels. It is important to keep in mind that this test is sensitive to many external factors, and is not meant to be used to diagnose disease but may indicate a general risk for atherosclerosis (cardiovascular disease). Higher values indicate healthier blood vessels. For Endothelial Function, any result of 1.6 or higher is considered "normal".

*** We have included the 25th-75th percentile measurement range for all CLEAR study participants, so you can compare your personal measurements. Note that 50% of subjects will have values outside of this range. Please note that ranges are meant only for interest and should not be used to infer any disease.

If you see a "X", this means there was a sampling problem from that session or the session was not completed.
A note on units of measure: mg/l = milligrams per litre
http://www.emedicinehealth.com/c_reactive_protein_blood_test_crp/article_em.htm#overview
YOUR HOME MEASUREMENTS:

<table>
<thead>
<tr>
<th>Average pollutant level over 7 days</th>
<th>With HEPA Filter in place</th>
<th>Without HEPA Filter in place</th>
</tr>
</thead>
<tbody>
<tr>
<td>Your home 4.5</td>
<td>Range of values* (25th - 75th percentile range in all CLEAR study homes)</td>
<td>Range of values* (25th - 75th percentile range in all CLEAR study homes)</td>
</tr>
<tr>
<td><strong>Particulate matter</strong>&lt;sup&gt;6&lt;/sup&gt; (PM&lt;sub&gt;2.5&lt;/sub&gt;) [μg/m&lt;sup&gt;3&lt;/sup&gt;]</td>
<td>&lt;hepa 1 home PM&gt;</td>
<td>X.XXX - X.XXX</td>
</tr>
<tr>
<td><strong>Levoglucosan</strong>&lt;sup&gt;7&lt;/sup&gt; [μg/m&lt;sup&gt;3&lt;/sup&gt;]</td>
<td>&lt;hepa 1 home levo&gt;</td>
<td>X.XXX - X.XXX</td>
</tr>
<tr>
<td><strong>Hopanes</strong>&lt;sup&gt;8&lt;/sup&gt; [μg/m&lt;sup&gt;3&lt;/sup&gt;]</td>
<td>&lt;hepa 1 home hopane&gt;</td>
<td>X.XXX - X.XXX</td>
</tr>
<tr>
<td><strong>Infiltration</strong>&lt;sup&gt;9&lt;/sup&gt; %</td>
<td>&lt;hepa 1 home infiltration&gt;</td>
<td>X.XXX - X.XXX</td>
</tr>
</tbody>
</table>

*We have included the 25<sup>th</sup>-75<sup>th</sup> percentile measurement range for the homes sampled in this study (N=XX), so you can compare the values from your home. Note that 50% of homes will have values outside of this range.

If you see a “-” in any cell, this means there was a sampling problem from that session or the session was not completed.

A note on units: all pollutants are expressed as a concentration in air: “ppm” (parts per million) means that there was 1 unit of pollutant per million units of air. Measurements of fine particulate matter are expressed as a mass per volume of air (1 μg = 1 part per 1,000,000 grams; 1 ng = 1 part per 1,000,000 grams).

Particulate matter: Higher values indicate higher levels of particles inside the home. Levoglucosan: 1,6-anhydro-β-d-glucopyranose, a cellulose combustion product, is a marker of wood smoke. Higher values indicate higher levels of woodsmoke inside the home. Hopane: 17α(H)-21β(H) - hopane an organic marker of traffic-related air pollution. Higher levels indicate higher levels of traffic-generated particles inside your home. Infiltration: Higher values indicate a greater contribution of air pollution from outdoor sources to indoor air.

How do my results compare with air quality standards?

There are no national indoor air quality standards and indoor concentrations of particulate matter are typically higher than those measured outdoors. For outdoor air, B.C.’s criteria for PM<sub>2.5</sub> of 25 μg/m<sup>3</sup> (averaged over 24 hours) established in 2009, remains in effect.

What can I do to minimize exposure to air pollution and improve the air quality in my home and community?

There are a number of things we can do as individuals to minimize exposure to air pollution and to improve the air quality in our homes and communities.

Personal exposure to air pollution can be reduced by altering behaviour. The BC Air Quality Health Index (<http://www.airhealthbc.ca/> ) is a scale designed to help you understand day-to-day changes in outdoor air quality and make decisions to protect your health by limiting short-term exposure and adjusting your activity levels during increased levels of air pollution. Increased use of active transportation, public transportation, or car sharing can reduce reliance on personal vehicles, thus reducing vehicle emissions, a major source of air pollution in greater Vancouver. When traveling, your route can influence your exposure to traffic-related air pollution. An online tool (<http://www.cyclevancouver.ubc.ca/> ) has been developed for greater Vancouver that allows users to select the cycling/walking route with the lowest traffic-related air pollution levels.

There are also options for reducing air pollution levels inside your home. As the results from this study show, HEPA filter air cleaners help reduce particulate matter concentrations inside homes.
by XX%, on average. You can also minimize the infiltration of outdoor pollution by keeping windows closed during high pollution periods (e.g. rush hour).

If you own a woodstove, both the type of stove and its operation are important for air quality. Newer, EPA certified woodstoves emit less pollution than older, non-certified stoves. Also, we urge all wood stove owners to take a training course to learn how to use your stove most efficiently.

The study website http://www.sfu.ca/clearstov/ will be updated with publications related to this study as they become available. No individual results will ever be posted on the website or reported in any publications. We have included a list of helpful web links on the last page of this letter, but please contact us should you have any further questions regarding the study or results (bkarlen@sfu.ca or Dr. Ryan Allen, allernr@sfu.ca)

Thank you again for contributing to a better understanding of the impacts of wood burning and traffic emissions on air quality and health.

Sincerely,

[Signature]

Dr Ryan Allen Principal
Investigator
Helpful Resources and Links:

1. SFU Cardiovascular Effects of Aerosols in Residences Study (CLEAR)
   www.sfu.ca/clearstudy/

2. The Lung Association
   www.lung.ca/protect-protegez/pollution-pollution_e.php
   Great resource about pollution and air quality, and what you can do to recognize and solve problems.
   Excellent information about air cleaning devices including HEPA filters under the Indoor Air section:
   http://www.lung.ca/protect-protegez/pollution-pollution/indoor-interieur/index_e.php

3. BC Air Quality Health Index
   http://www.airhealthbc.ca/

4. BC Health Files
   www.bchealthguide.org/healthfiles
   For information on air quality and pollution.

5. BC Air Quality
   http://www.bcairquality.ca/reports/pdfs/aqotable.pdf
   Provincial site devoted to air quality in BC.

6. Canada Mortgage and Housing
   http://www.woodheat.org/bis.html
   For an on-line guide to residential wood heating.

7. Environment Canada
   www.ec.gc.ca
   Clean Air section has information about wood heating and resources to help Canadians make informed decisions and take action to reduce air pollution.

8. Health Canada Air Quality Information
   Provides information about Canadian Research and guidelines covering air quality:
   www.hc-sc.gc.ca/ewh-semt/air/index_e.html

9. Excellent Information on HEPA Filters can be found at:
   The Lung Association:
   http://www.lung.ca/protect-protegez/pollution-pollution/indoor-interieur/cleaning-purificateurs_e.php
   U.S. Environmental Protection Agency: http://www.epa.gov/iaq/pubs/airclean.html

10. Recent publications on Traffic-Related Air Pollution and Health:
    https://circle.ubc.ca/bitstream/handle/2429/41542/2012-03-01%20Traffic%20and%20Health%20FINAL.pdf?sequence=1

11. If you are interested in learning more about cycling in urban areas: http://cyclingincities.spph.ubc.ca/
APPENDIX V: DWELLING INFORMATION
Home and heating questionnaire (to be completed by technician)

Home ID: ___________________  Date: ___________________

Participant ID: ________________

Second participant ID (if applicable) ________________

Sampling dates: ___________________and______________________.
DD/MM/YY - DD/MM/YY             DD/MM/YY - DD/MM/YY

1. Dwelling:
   a. Postal Code: ________________
   b. GPS Accuracy: ________________
   c. Latitude: ________________
   d. Longitude: ________________
   e. Elevation: ________________
   f. Age of home: ____ (year built: ________________)
   g. Substantial renovations
      (frame/windows/interior) year:
   h. Proximity to major roads (major road = 4 lanes):
      i. On a major road? Yes No
      ii. If not, within 50m of a major road? Yes No
   i. Type of building:
      i. single family  mobile/trailer  duplex  townhouse  apartment building
      ii. other:__________________________
   j. Floor (ground floor = 1st floor): ______ (single family home or townhouse = 1)
   k. Size of home:
      i. square footage: ________________
      ii. ceiling height: ________________
      iii. approximate volume: ________________
   l. Number of levels: ______ (including basement)
   m. Number of windows: ______ Number of windows that open: ______
2. Heating system:
   a. Primary heating system:
      i. Woodstove
      ii. Electrical
      iii. Gas
      iv. Forced Air/Furnace
         v. Hot Water/Radiator
         vi. Propane
         vii. Oil
         viii. Other: ________________
   b. Secondary heating system:
      i. Woodstove
      ii. Electrical
      iii. Gas
      iv. Forced Air/Furnace
         v. Hot Water/Radiator
         vi. Propane
         vii. Oil
         viii. Other: ________________

3. Wood stove (if applicable):
   a. Type of wood stove (if applicable):
      i. Fireplace
      ii. Conventional wood stove
      iii. Insert
      iv. Certified wood stove
      v. Pellet stove
   b. Wood stove brand and model: _______________________________________
   c. Approximate age of wood stove (years): ____________ (year of stove: ________)
   d. Location of wood stove in house (describe): ________________________________
   e. Fresh air intake installed on stove: yes no
   f. Chimney:
      i. Masonry Interior/Exterior Condition: ______________
      ii. Class A Interior/Exterior Condition: ______________
   g. Approximate proportion of household heating from wood:
      i. >90% ii. 50-90% iii. 20-50% iv. <20%
   h. Moisture content of two representative logs: __________  __________
4. Other house characteristics and emission sources:
   a. Estimate percentage of floor space covered with carpets (for the entire house): _______
   b. Do any you have any pets that reside INSIDE the home? Yes No Type: _______
   c. Are there any cigarette smokers residing at this residence? Yes No
   d. Kitchen:
      i. Stove type? Gas Electric
      ii. Range hood? Yes No
         1. If yes, is it used? Yes No
            a. If yes, how often? Always Sometimes Never
   e. Fireplace (in addition to wood burning appliance specified above):
      i. Present: Yes No
      ii. Type and number: Wood:_____ Gas:_______
   f. Chimney:
      i. Masonry Interior/Exterior Condition:______________
      ii. Class A Interior/Exterior Condition:______________
   g. Type of Garage:
      # of cars ______________________
      i. Attached (used for parking)
      ii. Attached (not used for parking)
      iii. Underneath building
      iv. Not attached to building
      v. No garage
APPENDIX VI: TIME-LOCATION-ACTIVITY DIARY
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**Weekly Medication & Activity Questionnaire**

**Participant ID:** ____________  **Session:** 1 or 2  **Questionnaire Date:** ____________

**Sampling session start and end date:** __________________________ - __________________________  

dd/mm/yyyy  

Please give the name, strength, and frequency of use for all medications, vitamins, and supplements that you have used in the past 7 days (since the last technicians’ visit).

**Prescription medication use:** (Those that were prescribed by a doctor and filled by a pharmacist; including: pills, dermal patches, eye drops, creams, salves, nasal sprays, metered dose inhalers, suppositories, and injections). The lists below should include medications you informed us of during the initial screening. Check/confirm strengths, etc. with participant screening questionnaire if applicable.

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<th>Data Entry Code</th>
<th>Medication Name</th>
<th>Strength</th>
<th>Frequency</th>
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<td>(Please include any use of „rescue“ medications such as Nitroglycerin, Asthma Inhalers, etc.)</td>
<td>(mg, mcg)</td>
<td>How many of these pills, applications, or inhalations did you take (use) in the past 7 days? If none, please write in “0”.</td>
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**Use of non-prescription medications, vitamins, or supplements:**

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<th>Substance or Brand Name</th>
<th>Type of Product</th>
<th>Strength</th>
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<td>(pill, cream, spray, etc.)</td>
<td>(mg, mcg)</td>
<td>How many of these pills, applications, or inhalations did you take (use) in the past 7 days? If none, please write in “0”.</td>
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Notes or other comments: (please use the last sheet if you need additional space)

_____________________________________________________________________________________________________________________________________________________________________________________________________________________________________________________
The following questions are intended to obtain more specific information about your activities and the characteristics of your home over the past 7 days (since our last visit to your home).

1. During the past 7 days, how much time did you spend doing the following during your travel time (including commute)?
   a. walking or biking ______ hours ______ minutes
   b. in a private car or taxi ______ hours ______ minutes
   c. on a bus ________ hours ______ minutes
   d. on a train (inc. SkyTrain) ______ hours ______ minutes
   e. other ________ hours ______ minutes please specify:________________________

2. What road/traffic condition best describes the roads on which you spent the majority of your travel time during the past 7 days?
   a. Side roads / neighbourhood streets
   b. Highways / major roads / arterials with:
      i. free-flowing traffic moving at the speed limit
      ii. heavy traffic moving below the speed limit
      iii. very heavy “stop and go” traffic
   c. N/A, I travel primarily by train or SeaBus

3. During the past 7 days, how much of the time were windows open in your home (include any open windows)?
   ________ hours ______ minutes OR ______ percent of the 7-day period

4. Did anyone (including yourself) smoke in your home in the past 7 days?
   □ Yes (skip to question 5)
   □ No (skip to question 5)
   □ Don’t Know (skip to question 5)
   a. How many hours total did smoking occur inside your home in the past 7 days?
   ________ hour(s)

5. During the past 7 days, has your home been smoky from cooking (e.g. burnt toast, barbecue, stir fry, etc.) at any time?
   □ Yes (skip to question 6)
   □ No (skip to question 6)
   □ Don’t Know (skip to question 6)
   a. How many hours total was your home smoky from cooking in the past 7 days?
   ________ hour(s)
6. During the past 7 days, in addition to the portable HEPA filters that we placed in your home as part of this study, was any other air cleaner/filter (stand-alone/portable or central) used in your home?

☐ Yes
☐ No (skip to question 7)
☐ Don’t Know (skip to question 7)

6a. What kind of air cleaner was used?

a. HEPA filter
b. Electrostatic precipitator
c. Negative ion generator
d. Ozone generator
e. Don’t know
f. Other, specify: ______________________

6b. Where is the air cleaner located?

______________________________

6c. During the past 7 days, how much of the time was the air cleaner used?

______________________________ hours ______ minutes

OR

______________________________ percent of the 7-day period

☐ ☐ Don’t know

7. [If the home has a woodstove] How much was the woodstove used during the past 7 days?

__________________ hours ______ minutes OR ______ percent of the 7-day period (if 0 skip to question 8)

7a. Estimated # of pieces of split firewood burned in the past 7 days?

7b. Type of wood burned (and proportions if more than 1 type burned)?

a. Pine — f. Maple ______
b. Spruce — g. Scrap lumber ______
c. Alder — h. Other: ______
d. Fir ______
e. Hemlock ______

i. Don’t know ______

8. How much time were the following used during the past 7 days in your home?

a. Air conditioning ______ hours ______ minutes OR ______ percent of the 7-day period
b. Woodburning fireplace ______ hours ______ minutes OR ______ percent of the 7-day period
c. Gas fireplace ______ hours ______ minutes OR ______ percent of the 7-day period
For each item below, please make an X at the place on the line that best represents how you feel now compared to how you usually feel. If you feel no different than usual, mark the place below “As Usual,” even if you usually do not have that symptom.

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APPENDIX VIII: HEALTH LOG
Health log sheet (to be completed by technician & subject)

Session X:  Home ID: ___________________  Participant ID: ____________
Measurement Date: ___________________  Technician: ____________
(today’s date)  dd/mm/yyyy

For Participant to answer (1 & 2):

1. Please indicate which of the following best describes your racial heritage (you may indicate more than one group):

   a. White
   b. Chinese
   c. South Asian (e.g., East Indian, Pakistani, Sri Lankan, etc.)
   d. Filipino
   e. Korea
   f. Aboriginal (First Nations) Including North American Indian, Metis, Inuit [Eskimo]
   g. Southeast Asian (e.g., Vietnamese, Cambodian, Malaysian, Laotian, etc.)
   h. West Asian (e.g., Iranian, Afghan, etc.)
   i. Japanese
   j. Latin American
   k. Black
   l. Arab
   m. Other — Please specify: ________________________________

2. Do you currently have a cold or any other known infection? __________________________

For Technician:

Session X Blood Draw Details

Confirm: 1. Has subject had anything to eat or drink (including water)? ____________________
2. Does subject have a history of fainting/troubles with blood draws?

3. Blood sample collected date: ________________________________
   i. Yellow tube collected  yes / no  # of tubes: _____
   ii. Lavender tube collected yes / no  # of tubes: _____

Before leaving Confirm:

- Consent signed
- Home and Heating Questionnaire completed
- Health Symptom Questionnaire reviewed
- Activity log completion reviewed
- Overview of next visit offered
Session 1:  Home ID: _______________  Participant ID: ____________
Measurement Date: _______________  Technician: ____________
(today’s date)  dd/mm/yyyy

ENDOPAT:
Subject’s dominant arm: (LEFT / RIGHT)

Describe setup:  room ___________  lying/sitting/reclining ___________
on bed/chair/couch ___________  lighting (type: low/med) ___________
Room temperature: ___________

Has subject had anything to eat or drink (including water)? ________________

| Blood Pressure  |
|-----------------|-----------------|----------------|
| (dominant arm)  | (dominant arm)  |
| Average Systolic| Average Diastolic| Heart rate |
|                 |                 | Notes      |

| EndoPAT         |
|-----------------|-----------------|----------------|
| (non-dominant arm)  | (non-dominant arm)  |
| Target cuff pressure  | Patient ID (Subject ID_session)  | RHI result |
| (systolic + 60; min. 200)  |  | Al result |
|  |  | HR result |
|  |  | Notes    |

Session 1 BLOOD Draw

Blood sample collected date: ____________________________

  i. Yellow tube collected yes / no  # of tubes: _______
  ii. Lavender tube collected yes / no  # of tubes: _______

Problems with blood collection? ____________________________

_________________________________________________________________
Session 2:  Home ID: ___________  Participant ID: _________  

**Measurement Date:** ___________  **Technician:** _________  
(today’s date) dd/mm/yyyy

Does subject currently have a cold or any other known infection? __________________________

Subject’s dominant arm: (LEFT / RIGHT)

Describe setup:  room ___________

  lying/sitting ___________

  on bed/chair/couch ___________

  lighting (type: low/med) __________________________

Room temperature:_________

Has subject had anything to eat or drink (including water)? __________________________

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<thead>
<tr>
<th>Blood Pressure</th>
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<tbody>
<tr>
<td>(dominant arm)</td>
</tr>
<tr>
<td>Average Systolic</td>
</tr>
<tr>
<td>Average Diastolic</td>
</tr>
<tr>
<td>Heart rate</td>
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<tr>
<td>Notes</td>
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<table>
<thead>
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<td>Notes</td>
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__________________________

Session 2 BLOOD Draw

**Blood sample collected date:**

  i. Yellow tube collected  yes / no  # of tubes: ______

  ii. Lavender tube collected  yes / no  # of tubes: ______

Problems with blood collection? __________________________